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CANCER ASSOCIATED WITH ACANTHOSIS NIGRICANS

REVIEW OF LITERATURE AND REPORT OF A CASE OF ACANTHOSIS NIGRICANS WITH CANCER OF THE BREAST

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NEW YORK

Acanthosis nigricans, rather widely discussed in dermatologic handbooks and journals,[1] has been strangely neglected in medical and surgical literature and in publications dealing with cancer. This is the more difficult to understand since in a great number of cases the occurrence of this characteristic cutaneous disease in itself suggests the presence of a coexisting internal cancer in the patient.

The association with cancer occurs in 49.74 per cent of all cases of acanthosis nigricans. So far 384 cases of the disease have been reported.

The study of a noncancerous disease associated with cancer under definite conditions offers great advantage to cancer research, which becomes wider by the additional investigation of the associated phenomenon and of its relationship to cancer. It is particularly fortunate that this associated phenomenon is represented by a well defined disease of the skin visible at early stages of development.

DEFINITION

Acanthosis nigricans is a benign disease of the skin which is clinically characterized by exaggeration of the cutaneous folds and brownish to blackish discoloration. It has a number of sites of predilection, of which the axillas are the most common (fig. 1). The mucous membranes may also be involved. The palms and plantar surfaces may show hyperkeratoses. Papillomas, pigmented spots and verruca-like changes may accompany the characteristic cutaneous changes. Histologic examination of the affected skin reveals hyperkeratosis, papillary hypertrophy, acanthosis and an increase in pigment, mostly in the basal layer.

Acanthosis nigricans occurs in two types: One type of acanthosis nigricans is associated with cancer of an internal organ, and is therefore falsely called malignant. The type of the disease not so associated is called benign. Of the 384 cases, 193 were of the benign and 191 of the malignant type. Cancer of the skin never develops from the cutaneous lesion of acanthosis nigricans, nor is it a cutaneous metastasis of an internal cancer, as has been described in connection with gastric cancer by Fasal and by Bourdillon. Since this paper was submitted for publication 11 additional cases of acanthosis nigricans have been reported, bringing the total number of cases to 395. Of these 11 cases, 5 were instances of the malignant type (Jeanneret; Silver; Sayer; Gunche, Iapalucci and Troncoso),

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1. Extensive reviews of cases are found in the monographs of Moncorps and Michy. Curth's paper (1936) contains a discussion of the causes of acanthosis nigricans.

Fig. 1.—Benign acanthosis nigricans of the axilla.

TABLE 1.—*Two Types of Acanthosis Nigricans*

	Malignant (Never Malignant in Itself and Not a Metastasis)	Benign (Sometimes Called Juvenile)
Incidence	About 50% of all cases	About 50% of all cases
Combination with cancer	Cancer in patient	No cancer in patient
Histology	Identical (see text)	Identical (see text)
Sex	Both sexes	Both sexes
Age at onset (no sharp division of types should be based on age)	Mostly middle-aged, also young and old persons	Usually at birth or in early years of life, but may appear or spread at puberty; caution with patients past second decade
Distribution	Symmetric	Symmetric or unilateral (neviform); Curth (1936) described a boy born with unilateral neviform acanthosis nigricans who showed symmetric acanthosis nigricans at and after puberty
Course	Mostly spreading; fatal outcome due to accompanying malignant tumor	Spreading at onset, later mostly stationary or regressing; duration indefinite
Familial cases	Not reported	Occasionally in one generation or two or three generations
Cases of "mixed" type	1. Baby born with unilateral acanthosis nigricans; later symmetric involvement of skin; death at age of 2 years from malignant tumor of abdomen (Halty, Correa Delgado and Volpé) 2. Thirty-six year old man with acanthosis nigricans of left elbow of fifteen years' duration; recent extension over body and mucous membranes; severe cachexia; cancer of stomach probable (Becker)	

3 were reported as cases of the benign type (Walzer; Franks; Garson and Sagnes) and 3 were mentioned by Lahiri without reference as to the type of the disease.

Table 1 briefly shows the characteristic qualities of each type. While acanthosis nigricans is generally distributed symmetrically, the benign form may occur on one

side of the body only. Many cases which have been listed as instances of ichthyosiform or acanthotic unilateral nevoid eruptions seem in fact to have been cases of benign acanthosis nigricans (Hitaka and others).

IDENTITY OF THE BENIGN AND THE MALIGNANT TYPE

The belief that benign and malignant acanthosis nigricans are the same is based chiefly on the identity of the histologic and macroscopic features of the two types.

Table 1 illustrates the possibility of transitional development: first, from unilateral benign acanthosis nigricans alone to a combination with symmetric benign acanthosis nigricans (Curth, case 1; Franks [2]); second, from unilateral acanthosis nigricans to symmetric malignant acanthosis nigricans (Becker); and it also shows the association with cancer of unilateral acanthosis nigricans in a baby dying from a malignant tumor (Halty, Correa Delgado and Volpé). Cases such as Becker's and Halty, Correa Delgado and Volpé's, showing characteristics of each type successively or simultaneously, will go far to strengthen the unitary conception of acanthosis nigricans.

How complicated classification of a case can be is illustrated by Freund's report of a 28 year old woman who had suffered from widespread symmetric acanthosis nigricans since the age of 9 years. When she was 27 multiple cancers of the breast rapidly developed. This case, of course, was of the malignant type, but eighteen years elapsed before the accompanying cancer manifested itself.

THE PRESENCE OF ACANTHOSIS NIGRICANS AND CANCER IN THE SAME PATIENT IS NOT COINCIDENTAL

Cancer is no mere coincidence in cases of acanthosis nigricans. Even if the so-called benign form is disregarded for the present, it is still true that 50 per cent of patients with a noncancerous disease suffer also from cancer. This is a much higher percentage of simultaneous occurrence with cancer than any other noncancerous disease would show.

In most cases of malignant acanthosis nigricans the two diseases become manifest at about the same time and run a parallel course. The cutaneous disease will show intensification and spreading to remote places at a time when the tumor is also progressive. There are several cases of malignant acanthosis nigricans on record in which simultaneous development of the two diseases assumed enormous proportions. I cite the following instances:

Case 1 (Hengstenberg).—A man aged 49 had suffered for five years from gastric disturbances (pain, belching and low gastric acidity). Acanthosis nigricans had been present on typical areas for five or six weeks. Examination revealed a large inoperable tumor of the stomach and an enlarged supraclavicular lymph node on the left side. Acanthosis nigricans gradually involved the skin of the entire body and part of the mucous membranes. Death occurred after one year. Autopsy revealed cancer of the stomach with involvement of the liver and also retroperitoneal cancer behind the stomach near the pancreas. Metastases of the third lumbar vertebra and of the bronchial, mediastinal and left supraclavicular lymph glands were found. Large tumor masses were seen at the upper part of the left kidney with destruction of the left adrenal. Acanthosis nigricans involved the skin and the mucous membranes.

Case 2 (Dubreuilh).—A man of 22 had suffered for many years from nausea and vomiting and acanthosis nigricans. For four months nausea and hyperpigmentation had been increasing. Examination revealed a large hard tender tumor in the left hypochondrium and five to six enlarged lymph nodes in the left supraclavicular fossa. Acanthosis nigricans became general-

2. Major Franks reports a case of a soldier who had had an epidermal nevus on the left side of the abdomen since birth and who had acquired symmetric acanthosis nigricans in the five months before he was examined. Exploratory laparotomy gave negative results. It seems that too short a time has elapsed to permit with any certainty classification of the type to which this patient's eruption belongs.

ized (the feet and the nails of the thumbs remained the only areas not involved). The tumor became larger, and generalized adenopathy was found. Death occurred after four months. Autopsy revealed peritonitis, ulcerated carcinoma of the pyloric region and tumorous lymph glands behind the stomach and in the mesentery. The lymphatic vessels of the intestines and the adrenals, the only internal organs examined histologically, were filled with neoplastic cells. The adrenals themselves were not destroyed. Acanthosis nigricans of the skin was verified histologically. Cancerous injection of the lymph vessels without inflammatory reaction of the neighboring tissue occurred in the deep skin or on the border of the hypoderm. These masses sometimes looked like a glandular cancer. Microscopic examination of all the internal organs was not undertaken, since death occurred during the first World War in a field hospital.

Hue speaks of *rapidité effrayante* with which in his case cancer of the uterus spread in a few weeks. During this period more and larger areas of skin showed acanthosis nigricans. In the cases of Lapa, Archangelskiij, Schalek, de Azua and Ducuing, who spoke of "acute" acanthosis nigricans, the cutaneous changes spread equally rapidly. In Scolari's and Dubreuilh's cases, the papillomatosis of the skin was especially conspicuous. In all of these cases rapid generalization of the cancer, which led to early death, accompanied the cutaneous changes.

The parallelism between the two diseases even goes so far that there is occasional regression, however transitory, of the cutaneous lesions after attempted removal of the accompanying tumor. It was seen in the cases of Kadono and Morino, Fuse, Spietschka (case 3), Hodara, Friedel, Kaposi and Joseph. Cancers in these cases involved various organs. Zollikofer reported that his patient noticed a decrease of the pruritus after resection of gastric carcinoma. In Spietschka's case, the only one of this series which was followed up, the lesions reappeared one and one-half years after operation for chorionic carcinoma at a time when a glandular metastasis was noticed. Reports of other cases do not mention even temporary improvement of acanthosis nigricans after operation.

One still may argue that a comparatively large number of middle-aged people will have cancer whether they are suffering from acanthosis nigricans or not. However, there are records of many young people with acanthosis nigricans and cancer (table 2). The significance of this high percentage of young people with cancer of the stomach especially becomes obvious when one realizes that cancer of the stomach is usually regarded as a problem for the age group over 40.

The following report is of a case which had been observed by Dr. Beatrice Kesten [2a] and by the surgical department of the Presbyterian Hospital of New York. Dr. Virginia Kneeland Frantz gave me all the information she could gather on the pathologic changes. The patient died at home. Permission for opening the thoracic cavity was not given.

In spite of the incomplete autopsy, the case merits publication because of the infrequently observed combination of acanthosis nigricans with cancer of the breast.

REPORT OF CASE

The patient, a married American woman 47 years old, was first examined in November 1938.

History.—Menses had started at the age of 11. The patient had one child, 18 years old, who was well. An operation for the removal of uterine fibroids, a salpingo-oophorectomy on the right side and an appendectomy were performed when the patient was 23 (1914). In 1932, cutaneous lesions on the body started to develop, one year after the diagnosis of recurrent fibroids had been made. For years she had noticed a swelling of the left lobe of the thyroid gland which seemed related to the menstrual period. For eight weeks a nodule in the right breast had been noticeable. Her chief complaints were abdominal pain and frequency of urination and, during the past month, unbearable itching and increasing roughness and darkness of the skin.

2a. The case is included in this series by special permission of Dr. Kesten.

TABLE 2.—*Cancer in Young People with Acanthosis Nigricans*

TABLE 2.—*Cancer in Young People with Acanthosis Nigricans*

	Authors	Age	Sex	Tumor	Verification of Malignancy	Classification of Tumor	Comment	Course
1	Halty, Correa Delgado and Volpé	2½	F	Abdominal tumor (inoperable)	Autopsy	Malignant tumor	.....	Died
2	Naruo, cited by Sekiba	9*	F	Cancer of stomach	Clinical picture	.....	Acanthosis nigricans for 5 years	No report
3	Lipskerof	17	F	Cancer of stomach (?)	Clinical picture	.....	.....	Cachexia
4	Herold, Kaufman and Smith	17	F	Gastric cancer with metastases	Laparotomy	Alveolar gastric carcinoma	.....	Died
5	Spietschka	20	F	Chorionic carcinoma	Operation	Chorionic carcinoma	.....	Metastasis
6	Dubreuilh	22	M	Gastric cancer with metastases	Autopsy	Cancer of stomach	.....	Died
7	Yamada	23	F	Cancer of pylorus	Clinical picture	.....	.....	No report
8	Flaskamp	23	F	Gastric cancer with metastases	Autopsy	Cancer of stomach with many metastases	.....	Died
9	Kobayashi	23	M	Cancer of liver (?)	Clinical picture	.....	Acanthosis nigricans since age of 12	No report
10	Masson and Montgomery (case 8)	25	M	Lymphosarcoma of stomach with metastases	Laparotomy	Lymphosarcoma of stomach	.....	Died
11	Lapa	26	M	Gastric cancer with metastases	Autopsy	Mucoid adenocarcinoma of stomach	.....	Died
12	Jakubson	27	F	Gastric cancer with metastases	Autopsy	Cancer of stomach	.....	Died
13	Archangelskiij	27	M	Gastric cancer with metastases	Autopsy	Cancer of stomach with many metastases	.....	Died
14	Freund; Brunetti, Freund and Sturli	27	F	Cancer of breast with metastases	Operation	Alveolar cancer of breast	Acanthosis nigricans since age of 9 years	No report
15	Barber	27	F	Cancer of stomach (?)	Operation	.....	Tumor inoperable	Alive
16	Masson and Montgomery (case 6)	29	M	Neoplastic process probable	Clinical picture	.....	Laparotomy 5 months before, negative	Died
17	Hodara	30	F	Cancer of breast	Operation	Cancer of breast	.....	Skin worse
18	Darier	30	M	Gastric cancer (inoperable)	Clinical picture	.....	.....	Metastasis
19	Masson and Montgomery (case 2)	30	M	Cancer of liver (?)	Laparotomy	Adenocarcinoma of liver (?)	.....	Died
20	Milian, Sauphar and Marceron	31	F	Abdominal cancer	Autopsy	Squamous cell cancer of lymph glands	Abdominal tumor not investigated	Died
21	Jordan, Schamschin and Dobrow	31	M	Gastric cancer with metastases	Operation	.....	.....	Died
22	Küttner (case 2)	32	M	Cancer of stomach	Roentgenogram and clinical picture	.....	Gastroenterostomy 2 years before	Patient worse

* Gougerot and Carteaud cited Mukai's observation of 14 patients who had malignant acanthosis nigricans before the age of 10. Mukai, however, listed these cases as benign.

Examination.—Examination revealed a brownish black discoloration of the skin with a few papillary growths in the axillary, antecubital and genitofemoral folds and on the vulva. "Corrugations" were also present on the hard palate. The palms showed hyperkeratoses. There was a pecan-sized swelling in the left upper lobe of the thyroid. In the right breast at 3 o'clock there was a lozenge-shaped mass 3 by 3 by 4 cm. which was freely movable and not tender and not definitely connected with the skin, nipple or thoracic wall. No dimpling of the skin was demonstrable. Enlarged axillary nodes could not be felt. The abdomen showed a well healed lower midline incision. The edge of the liver was palpable on deep inspiration. An irregular nodular mass in the pelvis extended upward almost to the umbilicus, somewhat to the left. The cervix appeared to be healthy. Routine laboratory examination did not furnish any contributory evidence. A diagnosis of acanthosis nigricans, tumor of the

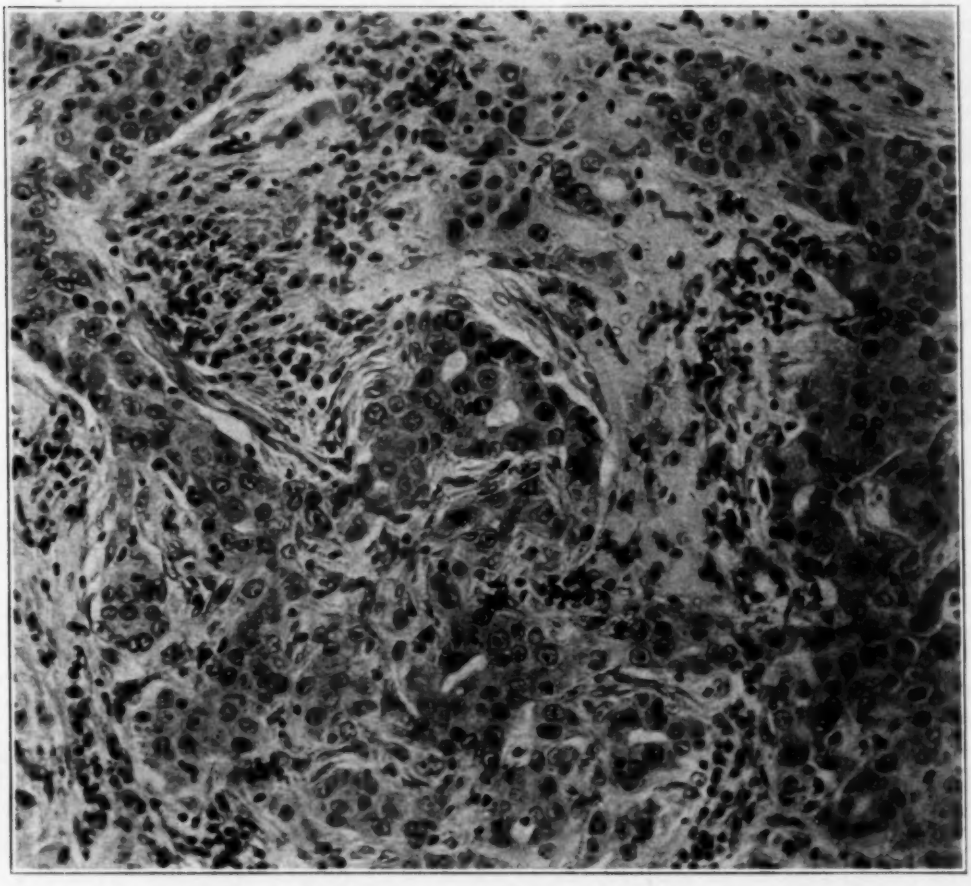

Fig. 2.—Cancer of the right breast.

breast (carcinoma?), tumor of the thyroid gland (nontoxic adenoma?) and fibromyomas of the uterus was made.

Course.—It was decided to explore the tumor of the breast before operating on the fibroids, and the operation was performed Nov. 17, 1938. On section the mass in the right breast was firm and white. There was no capsule, and there seemed to be definite infiltration of this tissue into the breast on the upper inner side. The gross diagnosis of carcinoma was verified by examination of frozen sections.

Complete right mastectomy with removal of pectoral muscles and axillary lymph glands was performed.

Microscopic Report.—Numerous large and small mammary ducts were lined or completely filled by tumor cells, numerous irregular clumps and cords of cancer cells and a few cancerous acini (fig. 2). Within the distorted and enlarged ducts likewise there was a definite tendency

to form rather well defined acini. Throughout the section extensive invasion of the connective tissue and fat was noted, and there was a slight to rather extensive infiltration with lymphocytes and large mononuclear cells. The individual tumor cells showed some variation in size and shape, the majority, however, being round, oval or polyhedral. Basement membranes were well preserved only in the ducts and acini. Elsewhere this structure was lacking and the tumor appeared to be growing irregularly. The nuclei showed about the same degree of variation as the cells. They were moderately chromatic and frequently had prominent nucleoli. Polarity was generally lost. Mitoses averaged about 1 in every two or three high power fields, and some were rather bizarre. At different points in the periphery relatively normal breast tissue was present. The section stained with mucicarmine failed to show any intracellular mucin.

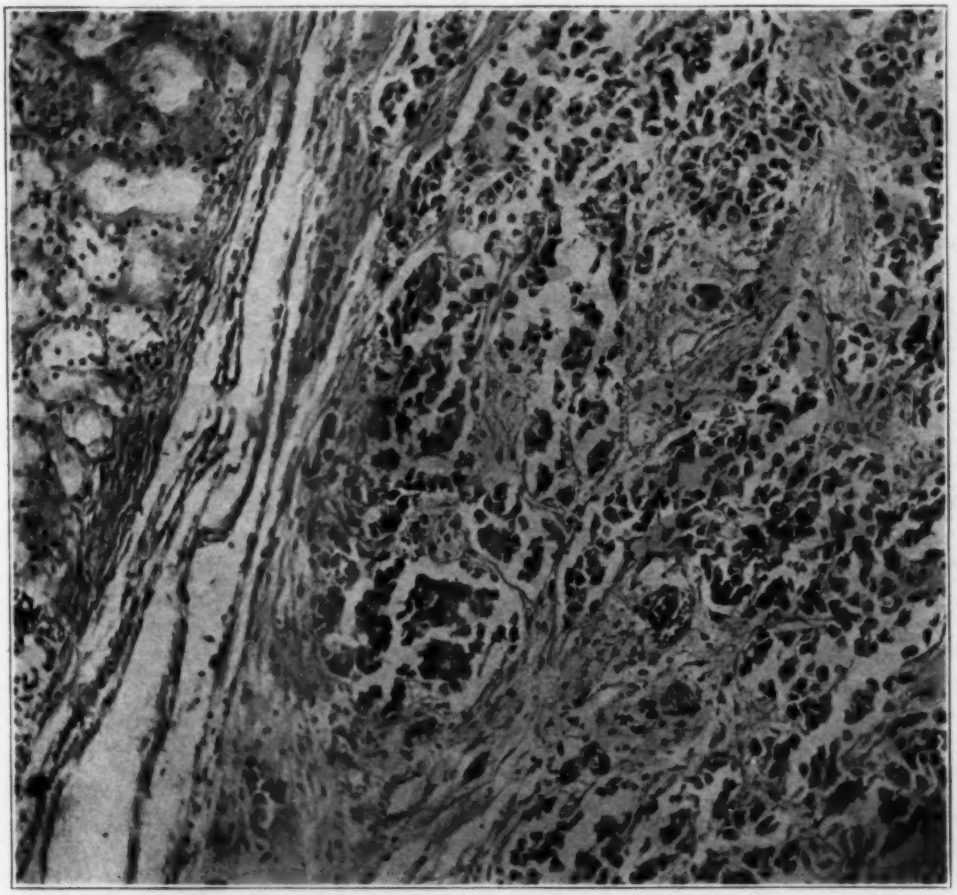

Fig. 3 (case 3).—Metastatic carcinoma of the left kidney.

Besides the tumor, there was evidence of mild mamillitis and chronic cystic mastitis of the right breast with rather marked epithelial hyperplasia.

Thirty-seven lymph nodes were found. Several appeared rather hard, and none contained tumor tissue.

The tumor was diagnosed as carcinoma (grade 2) of the breast, mostly intraductal. No invasion of lymph nodes, blood vessels or nerves was seen.

Further Course.—On December 1 supravaginal hysterectomy and left salpingo-oophorectomy were performed. The uterus had the size of a pregnancy of four and one-half months. The histologic diagnosis was fibromyomas of the uterus. Besides a practically normal left tube and follicular serous cysts of the left ovary, an old corpus luteum was found. At this operation pericholecystic postinfectional adhesions and a distended gallbladder were seen, but no signs of metastases.

In May and in November 1939, when the patient returned to the clinic for a check-up, no metastases of the tumor of the breast were found.

Four days after the removal of the right breast improvement of the itching was noted. The cutaneous lesions started to regress and became barely noticeable. When the patient was again seen, in March 1939, the cutaneous lesions had begun to reappear and to spread over wide areas. The papillary hypertrophy of skin and mucous membranes had reached bizarre dimensions. The patient was given six treatments with filtered roentgen rays during September and October on the most involved parts of the skin, with no effect.

In February 1940 a streptococcic sore throat developed, and the patient was rapidly going downhill. Before her death on June 6, she complained of considerable pain in the region of the liver. Permission was given only for removal of a section of the skin and for the

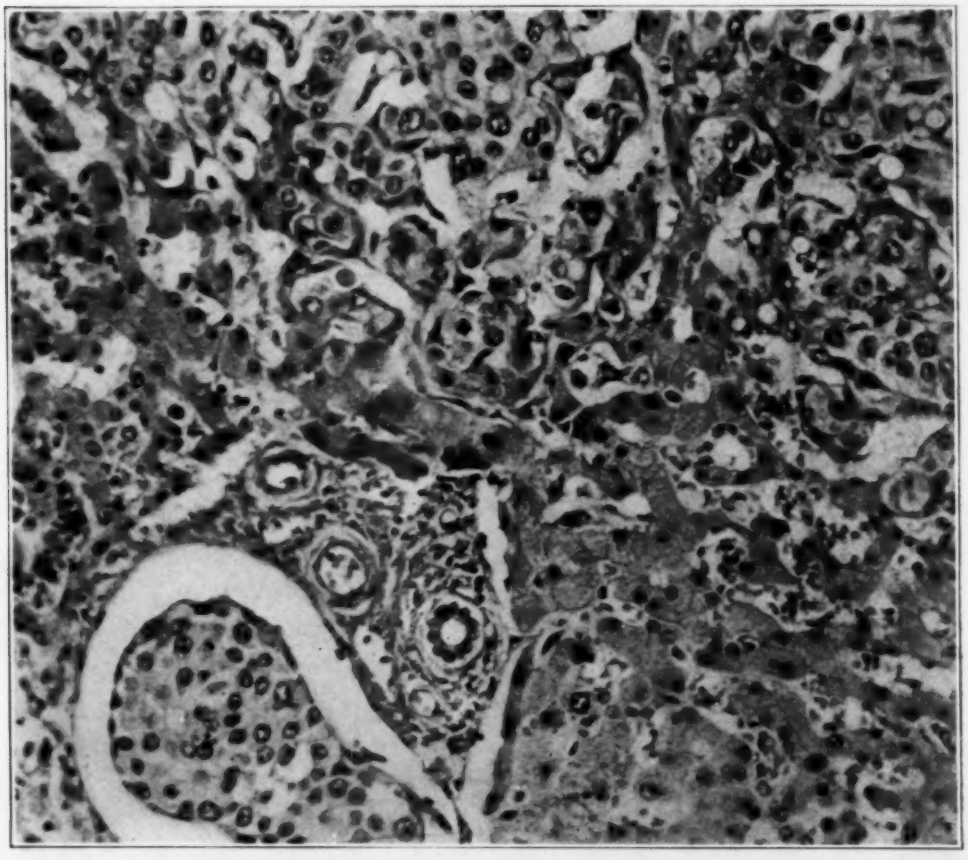

Fig. 4.—Metastatic carcinoma of the liver.

opening of the abdomen. The autopsy was performed by Dr. Morris Maslon, of Warren County, N. Y., who has permitted publication of his reports.

Autopsy.—When the abdomen was opened, the liver was found studded with carcinomatous masses. Carcinoma also was present in the left adrenal and in the upper pole of the left kidney (fig. 3).

Section of the liver (fig. 4) showed extensive invasion by a tumor similar to that in the breast, growing in the same cords and sheets, again with little tendency to glandular formation and with no mucin. Mitotic figures were again frequent.

Section of the adrenal (fig. 5) showed a small amount of adrenal cortex present. All the rest of the tissue was tumor. In portions of the tumor the cells showed no cohesion and appeared shrunken and fairly widely separated. In other portions, however, definite glandular arrangement was seen. The cells were large, for the most part polyhedral but sometimes columnar, and the nuclei were much more chromatic than those of the primary tumor. The lumens of the glands contained mucicarminophilic material, and droplets of this were found

in the cytoplasm of many of the cells. Such droplets were also found in the cells which showed less cohesion.

Sections of the skin (fig. 6) showed pronounced hyperkeratosis. The depressions between the sharp projections of the epidermis were filled with lamellated keratin-filled clefts. The papillary layer was wide. Pigmentation of the basal layer was striking. There were also scattered pigment-laden chromatophores in the papillary bodies. There was a slight perivascular infiltration in the corium.

Fig. 5.—Metastatic carcinoma of the left adrenal gland.

A diagnosis of acanthosis nigricans of the skin, associated with carcinoma of the liver, the left kidney and the left adrenal subsequent to carcinoma of the mammary gland was made.

Comment.—The cancer in this case was a primary cancer of the breast. This is the ninth case of mammary carcinoma associated with acanthosis nigricans reported in the literature. Fibromas of the uterus were also seen in Heath's case of mammary cancer. Their occurrence may be coincidental in view of the frequency

of uterine fibroids. The complete and early removal of the mammary cancer, apparently before regional metastasis had occurred, had inspired hope for a better result than was actually obtained. While nothing can be said about metastases in the thoracic cavity in the case reported here, widespread metastases were seen in the liver and in the left kidney and adrenal after a relatively short period. There was alveolar arrangement of the mammary cancer. Clumps, masses and strands of

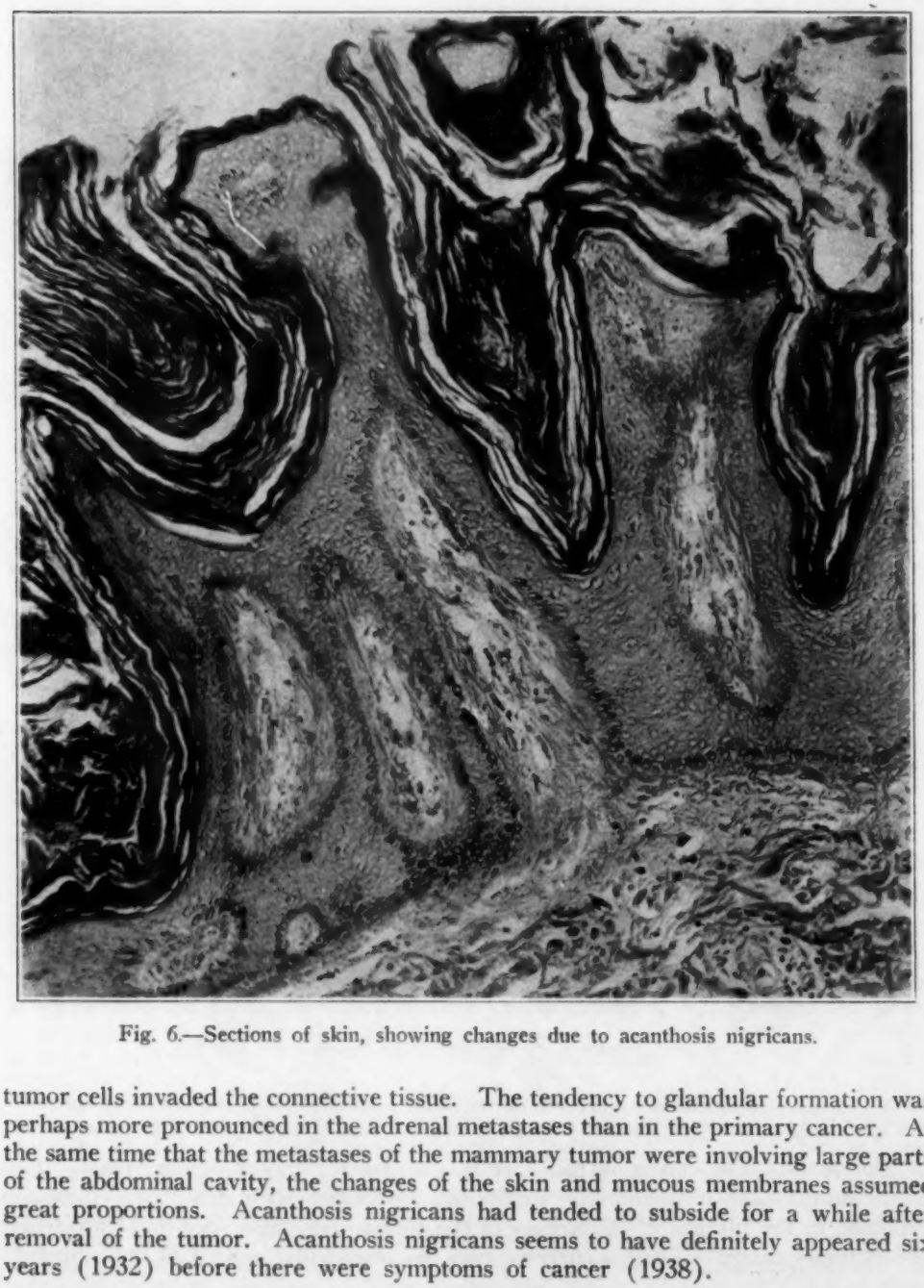

Fig. 6.—Sections of skin, showing changes due to acanthosis nigricans.

tumor cells invaded the connective tissue. The tendency to glandular formation was perhaps more pronounced in the adrenal metastases than in the primary cancer. At the same time that the metastases of the mammary tumor were involving large parts of the abdominal cavity, the changes of the skin and mucous membranes assumed great proportions. Acanthosis nigricans had tended to subside for a while after removal of the tumor. Acanthosis nigricans seems to have definitely appeared six years (1932) before there were symptoms of cancer (1938).

CANCER ASSOCIATED WITH ACANTHOSIS NIGRICANS

Incidence.—The incidence of acanthosis nigricans, and therefore also of cancers associated with it, is low. It is conceivable that in some cases of cancer subsequent appearance of acanthosis nigricans may have been prevented by the death of the patient. More records of abortive forms of the disease may reveal a greater incidence.

Abortive forms of acanthosis nigricans have been described by Miescher, Pollitzer, Barber (?) and Weber. I recently (1942) saw a patient with such a condition in consultation with Dr. Nathan Sobel and Dr. Charles Pines at the Central Clinic of the Bureau of Social Hygiene, of the Department of Health of the City of New York. A woman of 20 requested a test of her blood. During the examination, mild acanthosis nigricans of the sides of the neck and of both axillas involving the hairy parts and extending slightly beyond was found. The presence and duration of the cutaneous changes were unknown to the patient. She had menstruated at the age of 11 years 6 months. Her father had died in 1938 from cancer of the stomach. Her paternal grandmother had died recently in her sixties from cancer of the breast.

Cases of abortive acanthosis nigricans will have to be followed up carefully, and in the case in question the diagnosis will have to be verified.

Distribution.—Acanthosis nigricans has been described in all parts of the world. The first reports came from Germany (Pollitzer) and Austria (Janovsky). All other countries followed. Many cases of acanthosis nigricans occur in Japan. One Japanese author (Toyama) described 6 patients with acanthosis nigricans, 4 of whom suffered from cancer of the stomach; another (Sekiba) described 11 patients with acanthosis nigricans, 6 of whom had gastric cancer. One had a tumor of the liver, and the rest did not show any cancer. Javanese patients were described by Soetomo and by Polak. Most of the American reports concern white persons. American Negroes with acanthosis nigricans were described by Masson and Montgomery (case 5), Schamberg, Conrad and Rapp. The case of an African Negro was reported by Tessitore. Lately, several cases were observed in Mexico (Millán Gutiérrez) and South America (de Anduiza; Halty, Correa Delgado and Volpé; Balina, Braceras and Kaminsky; Castex and Facio; Muschietti and Vázquez; Roffo and Iapalucci; Orol Arias and Landabure; Sánchez Covisa and Brito Foresti and Vignale).

Sex and Age.—Stihl noted a ratio of 49.3 per cent female to 50.7 per cent male patients. The tables in this article give a percentage of 50.3 per cent female and 49.7 per cent male patients.

Table 2 shows that many young people suffer from malignant acanthosis nigricans. The greatest number of patients so affected, however, are middle-aged. Very old people with malignant acanthosis nigricans have been described. The patients of Nakamura, Perman, Tiefel, Lurie, Nicholas and Strandell were 70 years old, and those of Isaac and De Azua were 72. Scolari's was 74 and Wollenberg's 79. The average age is 40¾ years (Stihl).

Location of Cancer.—Darier's assertion that 80 per cent of all malignant tumors associated with acanthosis nigricans are abdominal is now only approximately correct. I found the percentage higher (92.67), since the only cases of non-abdominal cancer reported are 9 of mammary cancer (table 3), 3 of cancer of the lung (see table 4), and 2 in which the presence of a mediastinal tumor was suspected.

TABLE 3.—*Cancer of Breast in Patients with Acanthosis Nigricans*

Authors	Age	Site of Tumor	Duration	Verification of Tumor	Classification of Tumor	Extent of Tumor and Metastases	Course	Comment
Heath ?.....	63	.....	2 years	*	.....	.....	.....	Fibromas of uterus; removal of right breast 12 years previously, left breast 5 years previously
Freund; Brunetti, Freund and Sturli..	27	3 cancerous nodules in left breast	6 months	Operation	Adenocarcinoma	Metastases in axillary and supraclavicular glands	Alive	Acanthosis nigricans preceded cancer by 18 years
Hodara.....	30	.....	2 years	Operation	.....	.....	Alive; acanthosis nigricans worse	Acanthosis nigricans appeared after operation
Vereinigung Rheinisch-Westphälischer Dermatologen	57	.....	18 months after amputation	Operation	Carcinoma simplex solidum	Metastases	Alive	Onset of acanthosis nigricans after operation and irradiation of cancer
Matras.....	52	Right breast	8 months after extirpation	Operation; autopsy	Carcinoma solidum scirrhosum of breast; alveolar arrangement of metastases in liver	Metastases to liver	Died	.....
Boeck ?.....	52	Cancerous tumor in abdomen	2 years	No autopsy	Medullary cancer	Metastases in abdomen	Died	Operation for cancer of left breast 4½ years previously
Kutznitzky.....	41	.....	13 months	Autopsy	.....	Regional, abdominal, inguinal lymph glands, pleura, uterus, liver, skull, sternum	.....	.....
Sams.....	40	.....	.....	.....	.....	Carcinoma	Died	Carotenosis
Curth 2.....	47	Right breast	21 months	Operation	Alveolar arrangement	Liver, kidney, left adrenal	Died	Partial autopsy

* No operation was performed when acanthosis nigricans appeared; therefore the question remains open whether another cancer had developed or whether metastases had appeared as was indicated by some clinical observations.

Mukai gave the percentage of gastric cancer among the abdominal cancers as 58 to 61 per cent. I found it to be 69.86 per cent. In table 5 only those of the 102 cases will be listed in which there was cancer of the stomach with metastases. The remainder [3] were reported as gastric cancers without detailed information regarding possible metastases. The average duration of tumors of the latter group was 11.65 months, of the tabulated group, twelve months.

Cases of cancer located elsewhere than in the stomach were relatively few. There were 8 cases of cancer of the uterus (table 6) and 12 of cancer of the liver [4] (table 7). In 4 cases of cancer of the pelvis (table 8) and 8 of abdominal cancer (table 9) the primary tumor could not be precisely located. There were 2 cases each of cancer of the rectum (table 10) and cancer of the intestines (table 11). There was 1 case of cancer of the ovary (table 12) and 1 of probable primary renal cancer.[5] One questionable case of cancer of the pancreas was reported by Gilchrist (case 2) and 1 by Nägeli. One case suggestive of carcinoma of the esophagus was reported by Velikanoff. There was 1 case of chorionic carcinoma (table 13) and 5 in which metastases were present, but the primary site of the cancer was unknown (table 14).

TABLE 4.—*Cancer of Lung and Cancer of Chest in Patients with Acanthosis Nigricans*

Authors	Age	Sex	Verification of Tumor	Duration	Metastases	Site	Course
Petrini de Galatz.....	47	M	Autopsy	13 months	Pleura, hilus and tracheobronchial glands	Left lung	Died
Dore.....	..	..	Roentgenogram	.....	.....	Lung	.....
Wanderer.....	51	M	Roentgenogram; clinical picture	1½ years	.....	Mediastinum	Alive
Levin and Behrman..	50	M	Autopsy	2 years	Pleura, diaphragm, liver, kidney, peritoneum, intestines and right adrenal gland	Extensive carcinoma of left lung	Died

Type of Cancer.—In most of the reports on gastric cancer, adenocarcinoma was seen (Artom [case 1], Toyama [cases 1 and 2] and Roffo and Iapalucci [case 1]). This same type of arrangement was also found in tumor and metastases of the patient of Scolari (cancer of cardia), Mazzanti (mucoid adenocarcinoma of the gastric wall with metastases of the liver and glands) and Lapa (mucoid adeno-

3. Muschietti and Vázquez; Béron (case 1); Pautrier; Rille (case 1); Birch-Hirschfeld and Kraft (same case as Rille); Nicolas, Gaté and Lebeuf; Friedel; Ducuing, Masson and Montgomery (cases 4 and 5); Damblé; Frick (?); Guérault (?); Tokutomi; Kreibich; Küttner (case 2); Matras; Zollikofer; Fuse; Hermans and Schokking (?); Capelli (case 2); Asahi; Barber; Stanislawsky; Hissard (cases 1 and 2); Strandell (case 1); Becker; Berggreen; Naruo; Hirano; Darier (case 2); Mourek; van Leeuwen; Yamada; Makino; Ishiwatari; Takuwa; Ostwald; Montana; Feit; Bechet (2 cases); Jewsejeff and Posen (?); Kadono and Morino; Gilchrist; Yano; MacCormac (?); Tomasczewski; Kubo and Kohsaka; MacIntosh (?); Vidal.

4. The number of primary hepatic tumors given in this résumé seems very high in view of the rarity of primary carcinoma of the liver. As can be seen from the table, the diagnosis in many of the cases is chiefly based on clinical observations and has not been verified by operation, autopsy or histologic examination. The actual incidence of primary hepatic tumors in connection with acanthosis nigricans seems to be considerably lower.

5. The case reported by Dziobek as an instance of cancer of the kidney in a patient with acanthosis nigricans showed at operation papillomatous carcinoma of the left kidney. No report of further exploration or examination is given.

TABLE 5.—*Cancer of the Stomach with Metastases in Patients with Acanthosis Nigricans*

Authors	Age	Sex	Verification of Tumor	Duration of Tumor	Site of Tumor	Classification of Tumor	Extent of Tumor and Metastases	Comment	Course
Hengstenberg	49	M	Autopsy	One year	Stomach	.....	Retroperitoneal cancer behind stomach; metastases in liver, left kidney, left adrenal, left supraclavicular, bronchomediastinal lymph nodes, 3d lumbar vertebra	.....	Died
Dubreuilh	22	M	Autopsy (partial)	8 months	Pylorus	Metastases in alveolar arrangement	Supraclavicular and generalized adenopathy, lymphatic vessels of many inner organs and skin filled with tumorous masses	.....	Died
Artom (case 1)	63	M	Autopsy	About 1 year	Cardia	Ulcerated alveolar carcinoma	Adrenals, pancreas (?), glands in cardiac region and posterior wall of stomach	.....	Died
Perman (case 1)	70	F	No autopsy	10 months	Antrum	.....	Liver, 1 subclavicular gland	Marked polyposis of intestinal tract	Died
Perman (case 2)	55	M	Autopsy	5 months	Lesser curvature	.....	Retroperitoneal tumor, liver, kidney, right adrenal capsule, left adrenal (?), psoas muscle, mesenteric lymph nodes, spine	.....	Died
Toyama	60	M	Autopsy	3 years	Stomach	Adenocarcinoma (colloid)	Retroperitoneal lymph nodes (miliary tuberculosis of omentum)	.....	Died
Tesseraux	50	F	Autopsy	4-6 months	Pylorus	Partly scirrhous, partly cylindric cell carcinoma; glandular carcinoma in liver and lymph nodes	Right lung, liver, lymph nodes	.....	Died
Burgess	58	F	.....	.....	Lesser curvature	.....	Liver involved	.....	Died
Doutrelepont; Grouven and Fischer	34	M	Clinical picture	3 years	Stomach	.....	Liver involved	.....	Alive; worse
Périn	46	F	Roentgenogram	1 year	Stomach ?	.....	Liver involved	.....	Died
Sulzberger	63	M	Roentgenogram	3 months	Lesser curvature	.....	Liver involved	.....	Alive
Scolari	74	F	Autopsy	5 months	Cardia	Adenocarcinoma of cardia, in liver and lymph nodes	Esophagus, liver and peripancreatic lymph nodes and glands of hepatic hilus and lesser curvature	.....	Died
Lapa	26	M	Autopsy	18 months	Pyloroduodenal	Mucoid adenocarcinoma	Tumor in colon, duodenum; metastases in liver, gallbladder, pancreas, adrenals, kidney, supraclavicular, hilus, mesenteric, lumboaortic glands	.....	Died
Swartz; Swartz and Miller	41	M	Autopsy	6 months	Diffuse gastric cancer	.....	Liver, adrenals and retroperitoneal, cervical, inguinal and axillary lymph nodes	Clinical diagnosis had been metastatic sarcoma	Died

Janovsky	42	M	Clinical picture	Not given in detail	Stomach ?	.....	.....	Jaundice	Alive
Pribram	60	F	Clinical picture	2 months	Stomach	.....	Retroperitoneal and supraclavicular lymph nodes	Inoperable	Alive
Bogrow	48	F	No autopsy	6 months	Stomach ?	.....	Multiple nodules of liver	.....	Died
Klein	35	F	.....	At least 10 months	.....	.....	Recurrence and metastases	Far advanced	Alive
Milian, Sauphar and Marceron	31	F	Autopsy	3 months	Stomach ?	.....	Supraclavicular, subhepatic and prevertebral lymph nodes; liver involved	Squamous cell cancer in supraclavicular lymph node	Died
Jakubson	27	F	Autopsy	5 months	Stomach	.....	Liver, right kidney, right adrenal, all lymph nodes	.....	Died
Shiga	38	F	Autopsy	.....	Stomach	.....	Left adrenal; perigastric, retroperitoneal and supraclavicular lymph nodes	.....	Died
Mazzanti (case 1)	60	M	Autopsy	7 months	Pylorus	Ulcerated mucoid adenocarcinoma	Liver and lymph nodes	.....	Died
Addison (case 8)	53	F	Autopsy	3 months	Stomach ?	.....	Adrenals, mediastinal lymph nodes	.....	Died
Jordan, Schamschin and Dobrow (case 1)	31	M	Operation	8 months	Pylorus	.....	Tumor extending to mesocolon and pancreas; lymph nodes along lesser curvature, ligamentum hepatoduodenale, peritoneum and vessels of pelvis	.....	Died
Jordan, Schamschin and Dobrow (case 3)	60	M	Clinical picture	4 months	Stomach	.....	Liver enlarged	.....	Alive, unimproved
Lawrence	47	M	Clinical picture	3 months	Stomach	.....	Liver, spleen enlarged	.....	Alive
Darier (case 1)	34	F	Autopsy	6 years ? *	Lesser curvature	Ulcerated cancer of stomach	Tumor adherent to gastrohepatic ligament and to duodenum, liver, adrenals, spleen, pleura and peritoneum	.....	Died
Darier (case 3)	30	M	Clinical picture	Several years ? *	Stomach ?	.....	Left supraclavicular gland	.....	Alive
Barber	27	F	Operation	4 months	Stomach ?	.....	Multiple nodules of peritoneum	.....	Alive; tumor inoperable
Roffo and Iapalucci	51	M	Gastrectomy; autopsy	2 years, 4 months	Stomach	Adenocarcinoma	Tumor in hilus of liver, analogous to first tumor; metastases in mesentery	.....	Died
Archangelskij	27	M	Autopsy	.....	Stomach	.....	Prostate, bladder, adrenals, testes, pleura, lungs, cornea, hypophysis, pineal gland, bones of skull, solar plexus, many lymph nodes	.....	Died

* Not counted in statistics of duration of tumor.

TABLE 5.—*Cancer of the Stomach with Metastases in Patients with Acanthosis Nigricans—Continued*

Authors	Age	Sex	Verification of Tumor	Duration of Tumor	Site of Tumor	Classification of Tumor	Extent of Tumor and Metastases	Comment	Course
Bodenstein	38	F	Laparotomy	1 year	Stomach	.....	Mesocolon glands in mesentery and along vena cava	.....	Died
Küttner (case 3)	54	M	Clinical picture	3 years	Stomach ?	.....	Liver enlarged	.....	Alive
Masson and Montgomery (case 3)	38	M	No autopsy	20 months and over	Stomach	.....	Carcinomatosis (including liver ?)	.....	Died
Gordon	45	M	Operation	1 year	Stomach	Mucus-secreting scirrhous cancer of the stomach	Retroperitoneal and mesenteric lymph nodes	.....	Alive
Herold, Kaufman and Smith	17	F	Operation	10 months	Lesser curvature	Colloid cancer of stomach in alveolar arrangement	Mass in the omentum, firmly attached to the abdominal wall, spreading along the gastrohepatic ligament into the retroperitoneal tissue in the region of the celiac plexus and along the upper pole of the kidney; metastases in the preaortic nodes and along the colon	.....	Died
Lipskerof	17	F	Clinical picture	.....	Stomach ?	.....	Liver enlarged	.....	Alive; cachexia
Flaskamp	23	F	Autopsy	4 months	Stomach	Alveolar arrangement of metastases	Ovary, uterus, portion of liver, pancreas, adrenals, lymph nodes in mesentery and celiac plexus	.....	Died
Sekiba	64	M	Clinical picture	7 months	Pylorus	.....	Right and left supraclavicular glands	.....	Alive
Tsutsui	57	M	Clinical picture ?	14 months ?	Stomach ?	.....	Supraclavicular glands	.....	Not reported
Matsuura	38	F	Clinical picture	Not reported	Stomach	.....	Supraclavicular glands	.....	Not reported
Itazu	60	M	Clinical picture	Not reported	Stomach	.....	Supraclavicular glands	.....	Not reported
Sekiba and Saito	64	F	Clinical picture	.....	Stomach	.....	Submaxillary glands	.....	Not reported
Hallopeau, Jeanselme and Meslay	72	F	Clinical picture	Not given	Stomach ?	.....	Left supraclavicular gland	.....	Not reported
Ssutejev and Talalajev; Ssutejev, Klirikow, and Wainstein	55	M	Operation; autopsy	Not given	Stomach	.....	Metastases in solar plexus, adrenals and vertebrae	.....	Died
Castex and Facio	33	M	Operation	About 3 years	Stomach	Metastasis shows glandular cancer	Liver enlarged, metastases in supraclavicular glands and in rectovesical pouch	.....	Alive
Hess (case 1)	60	M	Clinical picture	18 months	Stomach	.....	Supraclavicular glands; liver ?	.....	Died
Isaac	72	M	Clinical picture	Not given	Stomach ?	.....	Melanotic tumor in esophagus; metastases	.....	Alive
Balassa	55	F	Clinical picture	Not given	Stomach ?	.....	Liver metastases	.....	Alive
Strandberg	50	M	Roentgenogram	Not given	Stomach	.....	Metastases in liver	.....	Alive; worse

carcinoma of stomach with pancreatic metastasis). Herold, Kaufman and Smith's patient and the patient in Artom's case 1 showed alveolar gastric carcinoma.

Metastatic cancer in alveolar arrangement was found in the ovarian and other metastases of Flaskamp's patient with gastric cancer and cancer of the mesenteric

TABLE 6.—*Cancer of the Uterus in Patients with Acanthosis Nigricans*

Authors	Age	Verification of Tumor	Duration	Extent of Tumor and Metastases	Classification of Tumor	Course
Hellerström.....	58	Clinical picture	Over 1 year	.....	.....	Alive; unimproved
Bruck.....	51	Operation	.....	Peritoneal metastases	.....	Alive
Grosz.....	58	Autopsy	Several months	Retroperitoneal and inguinal lymph nodes	Medullary carcinoma (ulcerated)	Died
Pollitzer.....	42	.....	.....	Abdominal metastases	.....	Died
Onozuka.....	64	No report *	At least 1 year	.....	.....	Alive
Hue.....	49	Operation	Several weeks	Tumor extending to vagina; pancreatic metastases (diabetes)	.....	Died
Milian, Périn and Babalian; Milian	53	Hysterectomy	Several months	.....	Cancer of body of uterus	Alive
Masson and Montgomery (case 1)	63	Operation	About 11 months	Tumor adherent to small bowel, bladder and broad ligament	Adenocarcinoma of body of uterus	Alive, skin worse

* Read only in abstract.

TABLE 7.—*Cancer of the Liver in Patients with Acanthosis Nigricans*

Authors	Age and Sex	Tumor	Verification of Tumor	Duration	Classification of Tumor	Course
Schröpl.....	61 M	Liver markedly enlarged	Clinical picture	.....	.....	Alive
Grace and Schwartz; Schwartz	46 F	Cancer of liver	Autopsy	About one year	Primary cancer of liver	Died
Tenneson and Leredde; Tenneson and Du Castel	42 M	Left lobe of liver indurated	.....	Four to five months	.....	Alive
Petrini de Galatz (case 3)	69 F	.....	Clinical picture	.....	.....	Alive
Strandell.....	..	.....	Autopsy	.....	Primary cancer of liver	Died
Béron.....	55 M	Cancer of liver ?	Clinical picture	Lately	.....	Alive; metastases in inguinal lymph nodes
Kobayashi.....	23 M	Cancer of liver ?	Clinical picture	No report	.....	No report
Masson and Montgomery (case 2)	30 M	Multiple nodules in liver	Laparotomy	Eight months	Adenocarcinoma of liver (primary ?)	Died
Corrado.....	52 M	Cancer of liver	No report *	.....	.....	No report
Ravogli.....	? F	Cancer of liver	.....	.....	.....	Died ?
Mazzanti (case 2)....	43 M	Cirrhosis of liver ?	Autopsy ?	.....	.....	Died
Mook and Drews.....	60 F	Cancer of liver	Operation	Two months	Adenocarcinoma of liver (primary ?)	Alive

* Read only in abstract.

glands and in the skin of Dubreuilh's patient, although in the primary cancer of the pylorus this arrangement was missing. The only evidence of a malignant neoplasm in Wild's case of acanthosis nigricans was a supraclavicular gland with

TABLE 8.—*Cancer of the Pelvis in Patients with Acanthosis Nigricans*

Authors	Age	Sex	Duration	Verification of Malignancy	Comments	Course
De Azua	62	M	Not given	Clinical picture	Acanthosis nigricans for 1 year	Alive
Schalek	55	F	8 months	No autopsy	Tumor in lower part of abdomen	Died
Thomae	34	M	(Lately)	Clinical picture	Tumor or metastases mostly in right side of pelvis	Alive
Tiefel	70	F	Not given	No autopsy	Metastases in inguinal glands	Died

TABLE 9.—*Abdominal Cancer in Patients with Acanthosis Nigricans*

Authors	Age	Sex	Duration	Verification of Tumor	Extent of Tumor and Metastases	Findings	Course
Pollitzer	62	F	1 month	No autopsy	.....	Ascites "Carcinoma occultum"	Died
Gaucher, Photinos and Evangelou	51	M	Several months	Clinical picture	Inguinal and subclavicular glands	Orange-sized tumor below umbilicus	Alive
Halty, Correa Delgado and Volpé	2½	F	21 months	Operation; autopsy	Tumor extending to pelvis	Inoperable abdominal tumor	Died
Collan	41	F	Not given	Clinical picture	.....	Abdominal tumor	Alive
Anderson	30	F	About 1 year	Unverified by laparotomy	.....	Tumor ?	Alive
Burmeister	36	M	9 months	Clinical picture; unverified by autopsy	.....	.....	Died
Galloway	About 30	F	3 months	Clinical picture	.....	Tumor in area of diaphragm	Alive
Masson and Montgomery (case 7)	37	F	4 years ?	Previous operations	Liver and spleen enormously enlarged, firm pancreas, enlarged lymph nodes in upper part of abdomen and along the vessels of back		Alive

TABLE 10.—*Cancer of the Rectum in Patients with Acanthosis Nigricans*

Authors	Age	Sex	Description of Tumor	Duration	Course
Eichhorst; Heuss	42	F	Large, ulcerated tumor	4 months	Alive
Little	60	M	Tumor of rectum	Not reported	Died

TABLE 11.—*Cancer of the Intestines in Patients with Acanthosis Nigricans*

Authors	Age	Sex	Verification	Duration	Course	Comments
Pollitzer	42	F	Clinical picture			
Brito Foresti and Vignale	48	M	Operation	18 months	Died	At an earlier laparotomy ulcerations of the stomach and tumors of the intestines were seen

TABLE 12.—*Cancer of the Ovary in a Patient with Acanthosis Nigricans*

Author	Age	Sex	Duration	Tumor	Verification of Tumor	Metastases	Course
Soetomo	Late fifties	F	7 months	Carcinoma of the left ovary (inoperable)	Operation	Intestinal and peritoneal	Alive; cachexia

TABLE 13.—*Chorionic Carcinoma in Patient with Acanthosis Nigricans*

Author	Age	Sex	Duration	Verification of Tumor	Course
Spietschka	20	F	21 months after confinement; 18 months after operation	Operation	Alive; metastases

carcinomatous growth of the glandular type. The metastasis in Castex and Facio's case showed glandular cancer. In Tesseraux' case of gastric cancer the metastases of the liver and the lymph nodes near the solar plexus were of the glandular type. In the lower lobe of the right lung intra-alveolar growth of cancer with hemorrhagic purulent inflammation was seen.

Adenocarcinoma of the uterus was present in Masson and Montgomery's first case. Grosz found an ulcerated medullary cancer of the uterus. Hepatic nodules in Masson and Montgomery's second case consisted of adenocarcinoma of grade 1. The hepatic tumor of Mark and Drews's patient and of the dog with acanthosis nigricans described by Curth and Slanetz was an adenocarcinoma.

There was alveolar arrangement of the mammary cancer described in this paper, as well as in Freund's case of multiple nodules of the breast. In Matras' case of mammary cancer the metastasis in the liver presented a clear picture of alveolar cancer.

Scirrhous cancer of the stomach existed in Gordon's and in Takuwa's case. Two cancers of the breast were described as solid scirrhous cancers (Matras,

TABLE 14.—*Glandular Metastases (Site of Primary Cancer Unknown) in Patients with Acanthosis Nigricans*

Authors	Age and Sex	Metastases	Classification of Tumor	Duration	Comments	Course
Wild	39 M	1. supraclavicular gland	Glandular cancer	.....	.....	Died; no autopsy
McDonald	64 F	Postauricular and cervical glands	Small round cell carcinoma	1 year	.....	Died; no autopsy
Archambault	54 M	Subclavicular gland	.....	.....	Gastric carcinoma suspected	
Markley	54 F	Subclavicular glands	.....	2 months	Laparotomy and roentgenogram of chest negative	Alive (cachexia)
Syrkin and Nikisain	27 M	Peritoneal and bronchial nodes; pancreas, lungs, adrenals, many bones	.....	About 1 year	Stomach free	Died; autopsy

Vereinigung Rheinisch-Westphälischen Dermatologen). Tesseraux dsecribed the gastric cancer in his case as partly scirrhous, partly cylindric cell carcinoma. The mother of the patient in the first case I described suffered from colloid carcinoma of the rectum. Mucoid cancer was noted in Lapa's and in Gordon's case.

Sarcoma Associated with Acanthosis Nigricans.—Klotz and Rohdenburg found in their case of acanthosis nigricans spindle cell sarcoma of the colon with metastases in the lung, liver, kidney, mesenteric lymph glands and skin. Swartz's case of metastatic sarcoma of the liver showed at autopsy diffuse cancer of the stomach with metastases in the retroperitoneal and cervical lymph glands, adrenals and liver (Swartz and Miller). Wile reported a case of acanthosis nigricans with generalized lymphosarcomatosis. Masson and Montgomery's patient (case 8), aged 25, suffered from lymphosarcoma of the stomach which already at operation extended to the mesocolon and was associated with metastases to lymph nodes. Nicholas described a case of retroperitoneal lymphosarcoma in which widespread metastases in abdominal organs, lymph nodes, bone, cutis and subcutis were found at autopsy. Sánchez Covisa described a case of acanthosis nigricans with diffuse lymphosarcoma of the stomach and metastases. There was no histologic verification of the diagnosis of lymphosarcoma.

Theory of Epidermal Cancer Refuted.—Milian, Sauphar and Marceron reported that in a case of malignant acanthosis nigricans squamous cell cancer of a supraclavicular gland occurred. They considered the neoplasm as of cutaneous origin. Since this possibility would be of fundamental importance, closer study of the evidence of the alleged cutaneous origin is indicated. The 31 year old woman had an intra-abdominal mass below the umbilicus. Enlargement of the supraclavicular gland and other glands developed. She also had secondary syphilis. Acanthosis nigricans remained uninfluenced by arsphenamine. Later the patient complained of pain in the abdomen, and jaundice developed. She died after three months. At autopsy typical acanthosis nigricans was found. Large masses of subhepatic and prevertebral lymph nodes and secondary nodules in the liver were seen. There also was a soft mass in the stomach. In view of the clinical evidence there seems to be insufficient proof for assuming the presence of a cutaneous cancer.

Cases of Acanthosis Nigricans and Cancer in Dogs.—Acanthosis nigricans with cancer has also been observed in dogs. In collaboration with Dr. C. A. Slanetz, I described the case of a dog with acanthosis nigricans and multiple primary cancer of the liver (figs. 7 and 8). Although in 13 other cases of dogs with acanthosis nigricans no cancer was found (the completeness of all examinations necessary is open to doubt), the dog described by Schindelka showed medullary cancer of the thyroid gland with metastases to the lung, liver, kidney and lymph glands.

High Malignancy of Cancer.—It is evident from the tables that all cancers associated with acanthosis nigricans are highly malignant. They occur relatively frequently in the young (see table 2), and in old people no mitigation is seen. The mortality rate [6] is high, and the duration is short. The average duration of cancer in cases of malignant acanthosis nigricans is eleven and ninety-five hundredths months.[7] Even in old persons it is in no case longer than a few years. Early inoperability of the tumor is clearly evident from a study of the tables.

Küttner's, O'Leary's and Masson and Montgomery's suggestion to perform an exploratory laparotomy in all cases of acanthosis nigricans, if a malignant lesion cannot be detected otherwise, is reasonable, but its practical fulfilment seems problematic. There are cases on record in which an early laparotomy was done and in which no tumor was discovered. The 29 year old patient of Masson and Montgomery (case 6), nevertheless, died five months later under circumstances which suggested the presence of a neoplastic process. Another patient whose laparotomy revealed nothing (Markley) soon became cachectic, and an increasing swelling of the lymph glands below the clavicle became evident. A malignant tumor in the thoracic cavity was suspected, but the suspicion could not be substantiated by roentgen examination.

In reviewing the fate of 3 patients with acanthosis nigricans who had been subjected to exploratory laparotomy, O'Leary concluded: "In other words, in our efforts to cure acquired acanthosis nigricans by the early removal of abdominal cancer we failed."

The present case emphasizes the importance of mammary cancer in association with acanthosis nigricans. Cancer of the breast and cancer of the lung, as has been reported by Petrini de Galatz and Dore, would not have been detected by

6. Statistics on the ultimate outcome cannot be given because many authors did not publish any reports on mortality.

7. The figure for the duration of the cancer was computed from reports regardless of whether the patient was dead or still alive at the time of the report.

opening of the abdominal cavity. Neither would the tumor in Wanderer's case of acanthosis nigricans, in which roentgen examination suggested the presence of a tumor in the mediastinum.

In other cases, operations were carried out early but the tumor recurred or metastasized later (Masson and Montgomery [cases 3, 4, 7 and 8]; Spietschka [case 3]; Küttner [case 2]; Castex and Facio; Bruck [carcinoma of uterus] Roffo and Iapalucci). In many cases (Flaskamp; Herold, Kaufman and Smith; Lapa; Bodenstein; Ostwald; Gordon; Halty, Correa Delgado and Volpé; Archangelskiij; Pautrier; Masson and Montgomery [case 2]) the tumor was more extensive than had been anticipated, and surgical removal was impossible.

Fig. 7.—Carcinomatous nodules in the liver of a dog with acanthosis nigricans (× ⅓). (Figures 7 and 8 were originally published with the article by Curth and Slanetz.)

The fact that acanthosis nigricans many times made its first appearance only after operative removal of the tumor (Roffo and Iapalucci; Matras [gastric carcinoma]; Onozuka; Kreibich; Béron [case 3]; Gordon, Hodara; Montana; Küttner [case 2]; Nicolas, Gaté and Lebeuf; Klein), after irradiation of the tumor (Hellerström) or after the two procedures combined (Matras [tumor of the breast], Masson and Montgomery [case 8], Vereinigung Rheinisch-Westphälischer Dermatologen) and that the patients rapidly got worse would also constitute a warning against expecting too much from an early operation. Nevertheless, all examinations which would detect a tumor at the earliest possible moment and which would lead to its removal are strongly advocated.

ETIOLOGY OF ACANTHOSIS NIGRICANS

Previous Concepts of the Disease.—Role of Sympathetic Nervous System: Authors in the past have emphasized the prime importance of one of the factors, mostly of cancer. Darier was the first to state, and many authors have followed his conclusions (among them Wile; Wise; Couillaud; Montgomery and O'Leary; Masson and Montgomery) that when metastatic cancer presses on the sympathetic nervous system its fibers become irritated. His other hypothesis was that cancer

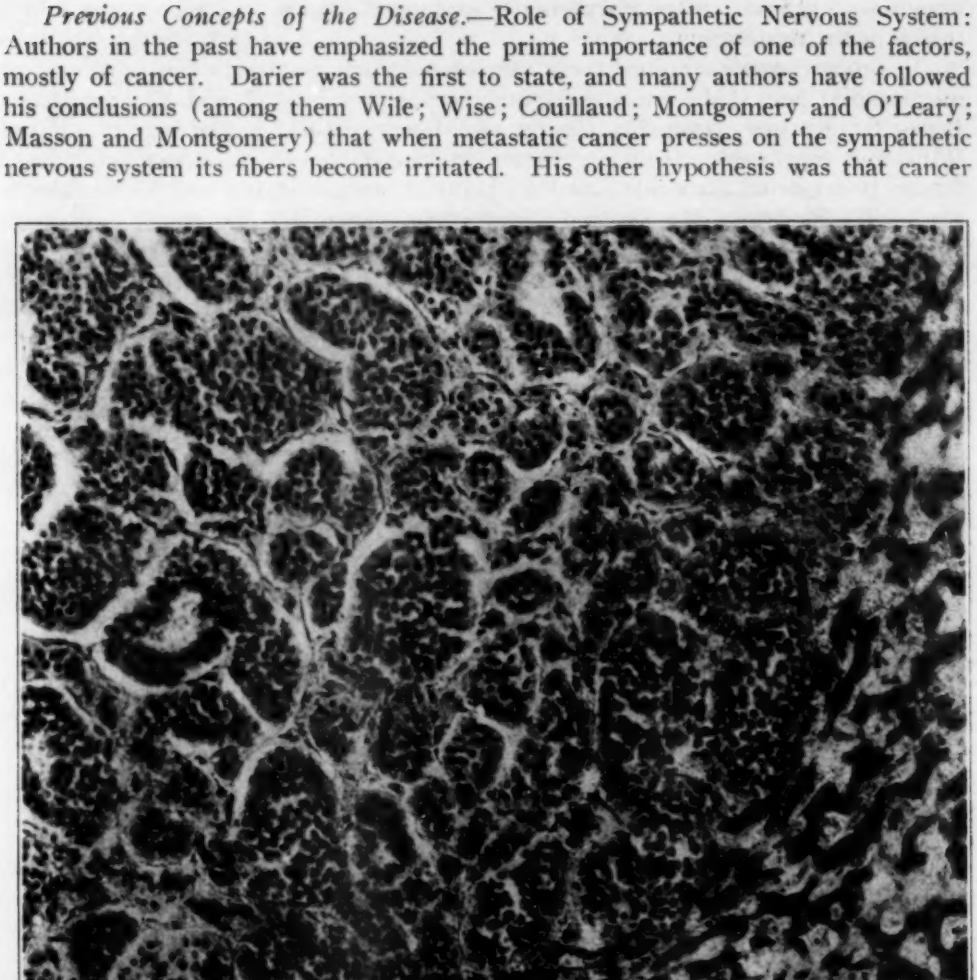

Fig. 8.—Cancer of the liver in a dog with acanthosis nigricans (× 100). Normal hepatic tissue is seen at the extreme right.

causes an autointoxication which produces acanthosis nigricans. This toxin was supposed to act on the sympathetic nervous system (Bloch).

Role of Adrenals: The autopsy in the case described in this paper revealed that the left adrenal was invaded by tumor masses. Other authors who report involvement of one or both adrenals are: Swartz and Miller; Swartz; Shiga; Pollitzer; Perman (case 2); Darier (case 2); Petrini de Galatz; Ssutejev, Klirikow and Wainstein; Archangelskiij; Nicholas; Dubreuilh (injection of lymphatics only); Flaskamp; Artom (case 1); Lapa; Kubo and Kosaka; Jakubson, Syrkin and Nikisain.

I agree with Halden Davis' statement that one of Addison's original cases is not an instance of Addison's disease but one of acanthosis nigricans. Case 8, in which the patient had typical cutaneous changes in the axillas (as suggested in a drawing) and around the umbilicus associated with a gastric carcinoma should indeed be regarded as a case of acanthosis nigricans with destruction of the adrenal gland. (Acanthosis nigricans was not yet recognized as a clinical entity in 1855.) In all these cases changes involving the adrenals were part of widespread metastases. The discovery of involvement of the adrenals seemed to establish the etiologic role of the sympathetic nervous system. Gordon, for instance, advocated this theory, although the autopsy in his case showed the adrenals to be free of cancer. There are also other cases of acanthosis nigricans with widespread metastases in which the adrenals were not involved in the cancerous process (Tesseraux; Arndt; Perman; Petrini de Galatz [lung tumor]; Scolari; Mazzanti; Toyama; Matras; Herold, Kaufman and Smith; Klotz and Rohdenburg). Perman rightly pointed out that the destruction of one adrenal capsule could not account for the complicated picture of acanthosis nigricans. Apparently, metastasis to the adrenals occurs in some cases of malignant acanthosis nigricans and not in others. It has no etiologic significance.

Endocrine Disturbances: Disturbances of the endocrine system have been extensively described in almost all reports of the benign type and even in a few reports of the malignant type of acanthosis nigricans. Most observers have agreed on their etiologic significance. In my first paper on acanthosis nigricans the etiologic role of the endocrine system was subjected to critical study. Theoretic considerations and actual records of cases speak against endocrine disturbances as a causative factor in acanthosis nigricans.

There is no one type of endocrine disturbance found in association with acanthosis nigricans. This observation is confirmed by recent reports which bring the previous review up to date.

Theodorescu observed amphotony and Goldschlag noted pluriglandular insufficiency. Yasuda and Ueki explained their patient's improvement following administration of solution of potassium arsenite (Fowler's solution) by the reduction of the epinephrine-like substances. Disturbances of the thyroid gland are frequently seen. One of Masson and Montgomery's patients (case 9) suffered from an adenoma of the thyroid gland. So apparently did the patient described in this paper. The patients of Behdjet, Masson and Montgomery (cases 1 and 10), Perman (case 3) and Flaskamp had goiter. Strumitis purulenta was found at autopsy in Grosz' patient with cancer of the uterus. Cancerous metastases to the thyroid gland as well as to other parts of the body occurred in Schindelka's dog with acanthosis nigricans.

Reports on diabetes are rather frequent. It was seen in the case of Millán Gutiérrez, Ravogli, Hermans and Schokking, Pollitzer and Lawrence. Hue explained the occurrence of diabetes in his patient as due to pancreatic metastases. Miescher and Hellerström described familial diabetes. Becker and Obermayer observed decreased tolerance for dextrose. The case was later presented by Rothman and Henningsen with the diagnosis of acanthoses nigricans and a questionable Cushing's syndrome.

Diseases Coincidental with Acanthosis Nigricans: Acanthosis nigricans may be associated with diseases other than cancer. They are listed in table 15 and include congenital defects and various acquired diseases. None of them occur in any significant percentage of cases. Furthermore, the association of acanthosis nigricans with these various diseases lacks the close interrelationship which exists between acanthosis nigricans and cancer.

TABLE 15.—*Diseases Coincidental with Acanthosis Nigricans*

Authors	Disease	Benign or Malignant Acanthosis Nigricans	Comments
Mumford	Deformed head	Benign	
Kémeri	Dwarfs, enlarged thyroid gland, 1 member with supernumerary nipple	Benign	Family (5 members)
Miescher	Cutis verticis gyrata, dental deformities, hypertrichosis, juvenile diabetes, debility	Benign	Family
Moura Costa	Debility and congenital syphilis	Benign	
Mourek	Debility	Malignant	
Filser	Debility	Benign	
Cavagnis	Debility	Benign	
Benedek and Csörsz	Idiocy and epilepsy	Benign	Acanthosis nigricans questionable
Goldbladt	Debility	Benign	Acanthosis nigricans questionable
Dóczy	Idiocy	Benign	
Weiss	Cryptorchism	Benign	
Ottkhine	Double cryptorchism	Benign	
Mukai	Friedreich's disease	Benign	
Lange-Cosack	Achondroplasia	Benign	Family
Pautrier and Hügel	Nevi, not commonly associated with acanthosis nigricans; one nevus with transformation into nevocarcinoma	Benign	
Hodara and Behdjet	Benign fibromatous nevi, covered with comedos	Benign	
Bernhardt	Multiple nevi and keratoma palmare and plantare	Benign	Family
Kutznitzky	Keratoma palmare and plantare	Malignant	
Dowling and Freudenthal	Trichoepitheliomatous changes, also psoriasis	Benign ?	Acanthosis nigricans questionable
Hamdi and Reschad	Budlike changes about the sweat glands, dermoid cyst	Benign	Acanthosis nigricans questionable
Jewsejeff and Posen	Darier's disease	Malignant ?	
Theodorescu and Comsa	Epidermolysis bullosa	Benign	
Knowles	Epidermolysis bullosa	Benign	
Fox	Psoriasis	Benign	Acanthosis nigricans questionable
Wolff	Psoriasis	Benign ?	
Majocchi	Urticaria	Benign	
Scarpa	Urticaria	Benign	
Lehner	Sclerema adultorum	Benign	
Patrassi	Sclerema adultorum	Benign ?	Acanthosis nigricans questionable
Tzanck and Levy	Sclerema adultorum	Malignant ?	
Bernhardt	Bowen's disease, independent of the lesions of acanthosis nigricans	Benign	
Behdjet	Lichen ruber acuminatus	Benign ?	
Rasch	Pityriasis rubra pilaris	Benign	
Balina, Braceras and Kaminsky	Pityriasis versicolor, acquired syphilis and obesity	Benign	
Milian	Condylomata acuminata	Malignant	
Milian, Sauphar and Marceron	Syphilis, acquired	Malignant	
Bonnet	Syphilis, acquired	Benign	Acanthosis nigricans questionable
Caussade, Lévy-Franckel and Juster	Syphilis, acquired	Benign	Acanthosis nigricans questionable
Touraine and Renault	Syphilis, acquired, and vitiligo	Benign ?	
Ingram	Syphilis, acquired, tumor in pharynx	Malignant ?	
Herold, Kaufman and Smith	Syphilis, acquired	Malignant	
Lawrence	Syphilis	Malignant	
Perman (case 3)	Syphilis, acquired ?	Malignant ?	Acanthosis nigricans questionable
Bruck	Syphilis, acquired	Malignant	
Millán Gutiérrez	Syphilis, acquired ?	Benign ?	
Muschietti and Vázquez (case 2)	Syphilis, congenital	Benign	
de Anduiza	Syphilis, congenital	Benign	
Mayo Clinic, and Masson and Montgomery (case 10)	Syphilis of the central nervous sytem; goiter	Malignant ?	
Crocker, R.	Old scrofulous abscesses	Benign ?	
Toyama	Miliary tuberculosis of omentum	Malignant	
Knowles, Sidlick and Ludy (case 2); Weidman	Tuberculosis of peritoneum	Benign	
Solla Casalderrey	Tuberculosis of lungs	Benign	
Mazzanti	Tuberculosis of lungs	Malignant	Carcinoma of pylorus
Wollenberg	Tuberculosis cutis verrucosa	Malignant ?	
Alkiewicz	Periarteritis nodosa	Benign ?	Acanthosis nigricans questionable
Matras	Parkinsonism	Benign ?	
Soetomo	Acromegaly with tumor of hypophysis	Malignant ?	
Pollitzer	Alcoholism	Benign	
Hyde and Montgomery	Alcoholism and obesity	Benign	
W. Jadassohn	Obesity	Benign	Family
Rapp	Obesity	Benign	
Butterworth	Obesity	Benign	
Sayer	Obesity	Benign	
Senear	Obesity; syphilis ?	Benign	
Becker and Obermayer	Obesity	Benign	
Jeanneret	Aurantiasis palmarum	Malignant	

Local Disturbances Preceding Cancer: Peptic and duodenal ulcer, constipation and vague gastric symptoms of long standing have been described in many cases of gastric carcinoma.

Perman stated that in the first of his 3 cases cancer developed secondarily in polyposis which had been present in the rectum and bladder. Gastric carcinoma was suspected on roentgen examination. Autopsy was not performed. The polyposis may perhaps be explained by involvement of the mucous membranes with acanthosis nigricans. Such was seen in the esophagus in the cases of Scolari, Tesseraux (also in nose, larynx and pharynx), Archangelskiij, Ssutejev and Talalajev (also in rectum) and Toyama (conjunctiva) and was described as benign tumors of acanthosis nigricans in von Bergmann and Staehelin's "Handbook of Internal Medicine."

Activation of Acanthosis Nigricans.—In some cases acanthosis nigricans tends to subside after treatment of the tumor and then to reappear in full or even increased strength, with a recurrence or metastasis of the tumor. A study of this phenomenon suggests that some properties of the tumor may activate acanthosis nigricans, influencing it either directly or indirectly.

Improvement following nonspecific treatment, i. e., liver extract (Danbolt, Strandell), resection of the cervical ganglion (Mukai), arsphenamine (Bonnet) and thyroid extract (White; Rosenthal; Klotz and Rohdenburg; Knowles and Ludy; Yasuda and Ueki) shows that acanthosis nigricans can be influenced by methods which may not attack the accompanying cancer directly. A few cases of acanthosis nigricans (without cancer) also showed a limited response to these therapeutic measures.

If treatment of the tumor is attempted, the tendency to disappearance of acanthosis nigricans is not evident in all cases. It seems to depend on the extent to which the cancer (or carcinogenic substances or substances produced by the cancer) could be eliminated. These substances are certainly not the only determining factors, but they may play an activating role in the reproduction of the cutaneous lesion (Moncorps, Gaucher, Kyrle).

Role of Puberty.—In the benign form the same role of activation seems to be played by one of the sex hormones. In reviewing the literature I was surprised at the large number of patients with benign acanthosis nigricans in whom the cutaneous lesions of acanthosis nigricans appeared at puberty or in whom preexisting lesions began to spread.[8] It may also happen, as in the case of the young boy which I published in 1936, that symmetric acanthosis nigricans developed at puberty in a person who had had unilateral acanthosis nigricans since birth. Hellerström's observation of a man in whom acanthosis nigricans disappeared after castration seems to prove the same: One of the hormones of the sex glands is necessary for the reproduction of acanthosis nigricans. That sex hormones and substances produced by or related to cancers would play the same role (of activa-

8. Tolmach; Allen; Weiss; Frankenstein and Juliusberg (?); Artom (case 2); W. Jadassohn; Miescher; Hyde and Montgomery; Wertheimer; Boggs and Roblee; Sayer; Kinoshita; Butterworth; Wieder; Balina, Braceras and Kaminsky; Mayo Clinic; Ottkhine; Petrini de Galatz (case 1); Jacquet and Delotte; Jacquet; Frühwald (?); Pawlof; Chirivino; Mžareuloff; Goldschlag (?); Wile; Danbolt; Béron (case 2); Rasch; Brezovsky; Baliszkaja; Spietschka (case 1); Rille (cases 2, 3 and 4); von Leszczynski; Hodara and Behdjet; Conrad (?); Pechur and Čerkes (case 2); Rapp; Masson and Montgomery (case 10); Smith; Knowles, Sidlick and Ludy; Orol Arias and Landabure (acanthosis nigricans questionable); Behdjet (1932, case 2; 1934); Marziani (?); Jordan, Schamschin and Dobrow (case 2); Thomson; Senear.

tion) is not surprising in view of the importance of sex hormones as the cause of certain cancers (Lacassagne) and the close chemical relationship between sex hormones and some carcinogenic substances.

Importance of Cancer.—Endocrine disturbances apparently have no etiologic significance. The importance of pressure on the sympathetic nervous system due to abdominal cancers can be discounted, since some of the associated cancers are extra-abdominal. Furthermore, autopsies have failed to reveal involvement of the sympathetic nervous system, and there is a high incidence of the benign form of the disease, in which intra-abdominal changes are not present.

In studying the etiology of acanthosis nigricans one has to consider the benign type as well as the malignant. The histologic and clinical identity of the two types and the occasional transition from one to the other demand the same etiologic explanation.

The extremely high percentage of cancer associated with acanthosis nigricans and the parallel course of the two diseases are indicative of an intricate relationship between them. The study of malignant acanthosis nigricans cannot disregard cancer as an essential factor.

But does not the lack of cancer in the benign type, which represents one half of all cases of acanthosis nigricans, cast doubt on its etiologic significance?

The character of a genodermatosis, so much more obvious in benign than in malignant acanthosis nigricans, tends, indeed, to overshadow any other factor which may play a significant role in the origin of the disease.

Genetic Relationship Between Cancer and Acanthosis Nigricans.—Family Histories of Patients with Acanthosis Nigricans: Cancer can still be detected in cases of benign acanthosis nigricans. It is represented here by the involvement of a family member. Moncorps and Stihl have already stressed the frequent occurrence of carcinoma among the antecedents of patients with acanthosis nigricans. Table 16 gives data on cancer in the family histories of such patients. Among the immediate antecedents of patients with both the benign and the malignant form is found the same type of cancer (with the exception of cancer of the larynx [Matras]) which has been observed directly associated with malignant acanthosis nigricans. Cancers of the stomach, the liver, the uterus, the rectum and the breast have been reported. More data not only on the antecedents but also on the descendants and siblings of these patients will be needed in order to evaluate better the incidence of cancer in relatives of patients with acanthosis nigricans.

It cannot be denied that many antecedents are found without cancer, but it should not be overlooked that they may have died before cancer developed or that the phenotypic manifestation of cancer may have been influenced or even suppressed by other factors. In malignant acanthosis nigricans these opposing factors apparently are much less, or only temporarily, effective.

If we assume that the relationship between acanthosis nigricans and cancer is genetic, cancer keeps its significance even for a form of the disease in which it is absent from the clinical picture.

Furthermore, genetic relationship would explain the strange fact that two related factors occur in one instance combined in one person (malignant type), while in the other instance they occur dissociated in two separate but genetically related persons (benign type).

Any genetic relationship between two factors leads to the question of the hereditability of each. Inheritance of acanthosis nigricans has been observed. Familial cases with involvement of as many as three generations have been noted.

In these cases acanthosis nigricans remained benign and did not assume the features of the malignant form (rapid spreading and a course parallel to that of an internal cancer).

Inheritance of cancer associated with acanthosis nigricans can be noted in several cases (table 16). This study will have to be made more complete and will have to include histories not only of antecedents but of descendants of patients with malignant acanthosis nigricans before definite conclusions as to the type of hereditary transmission can be drawn.

TABLE 16.—*Data on Cases of Acanthosis Nigricans in Association with a Family History of Cancer*

Author	Acanthosis Nigricans		Family History of Cancer	
	Age in Years	Sex	Relative	Cause of Death
Baliszkaja	16	F	Father	Cancer of stomach
von Leszcynski	16	F	Father	Cancer
Asahi	69	M	Father	Cancer of stomach
Wieder	10	F	Maternal grandmother	Cancer of stomach
Brünauer	23	F	Father	Branchiogenic carcinoma
Curth	15	M	Mother	Colloid carcinoma of rectum at age of 36
Ogino	?	M	Father	Cancer of stomach
Liebner	38	M	Mother	Carcinoma of breast
Tominaga and Harada	60	M	Paternal granfather	Cancer of stomach
Radaeli	51	M	Father and brother	Cancer of liver
Becker and Obermayer; Rothman and Henningsen	11	F	Father	Branchiogenic carcinoma at age of 37
Guérault	39 Cancer of stomach probable	F	Father and Sister of father	Intestinal (cancer ?) at 62 Cancer of stomach
Grace and Schwartz	46 Primary cancer of liver	F	Father	Cancer of rectum
Lapa	26 Cancer of pylorus	M	Father	Cancer of liver at 64
Mazzanti	60 Adenocarcinoma of pylorus	M	Father	Neoplasm at 63
Darier	30 Cancer of stomach	M	Father	Cancer of stomach (?)
Matras	52 Carcinoma of breast	F	Father	Carcinoma of larynx
Heuss; Eichhorst	42 Cancer of rectum	F	Father and Sister	Cancer of stomach at 54 Cancer of breast at 36
Tiefel	70 Cancer of pelvis (?)	F	Mother	Cancer of the uterus in the sixth decade
Thomae	34 Tumor of pelvis	M	Father	Jaundice (tumor ?) at 68
Velikanoff	50 Cancer of esophagus (?)	M	Brother	Cancer
Jordan, Schamschin and Dobrow	31 Cancer of stomach	M	Mother	Cancer of stomach

Glandular Cancers: The fact that glandular cancers are found is noteworthy in this connection. The hereditary factor is of more importance in glandular than in squamous cell cancer (Schinz and Buschke).

Chronologic Independence of the Two Diseases: In the case described in this article acanthosis nigricans seems to have appeared definitely six years (1932) before there was evidence of cancer (1938). This would be a long interval, but it is not the longest one on record, by far. We have already mentioned Freund's case of a 27 year old woman in whom cancer developed after acanthosis nigricans had been present for eighteen years. Artom described a 63 year old man in whom gastric cancer developed after he had been under observation for fifteen

years because of acanthosis nigricans. Van Leeuwen's patient, a 42 year old man, had had slowly progressive acanthosis nigricans for ten years before cancer of the stomach developed.

It seems that the two diseases are usually discovered at about the same time, or, since the early changes in the skin are more easily perceptible than the neoplasm, there is an apparently slightly earlier recognition of acanthosis nigricans. However, there are also reports of its appearance subsequent to the removal of the tumor (Tesseraux, Klein, Damblé, Hengstenberg, Lapa, Friedel, Doutrelepont, Pautrier, Soetomo, Hissard [*a*],[9] Ostwald, McDonald [after manifestation of glandular metastases], Sánchez Covisa). Too great an interval between initial cancer and subsequent acanthosis nigricans would be improbable on account of the highly malignant character of the tumor.

I have dealt extensively with the problem of chronologic sequence of acanthosis nigricans and cancer in order to show that no definite rule about it can be set up. Sometimes acanthosis nigricans precedes cancer by a long time, sometimes by a short time. Frequently they start simultaneously. The onset of acanthosis nigricans rarely follows the manifestation of cancer. Conditions seem to vary from case to case, and one would have to conclude that neither disease is the primary one to which the other is a consequence. A genetic relationship between the two would not designate either disease to be the more important causative factor.

CRITERIA OF BENIGN AND MALIGNANT ACANTHOSIS NIGRICANS

If confronted with the problem whether a patient with acanthosis nigricans alone suffers from the benign type or from the type eventually associated with internal cancer, it is important to consider the following points:

1. The age of the patient at the onset of the disease is significant. The benign type will appear at birth or during the early years of life or at puberty. (Bernhardt recorded an exceptional occurrence in a family in which members of three generations showed the first signs of acanthosis nigricans at the age of 35.)

In cases of benign acanthosis nigricans the cutaneous lesions remain stationary and no cancer develops. The cases on record in which patients remained free from internal cancer for the longest period of time are those of Pautrier and Hügel, forty-four years (from the fifth to the forty-ninth year); Spietschka (case 2), 41 years (from the third to the forty-fourth year); Cavagnis and Giovanni, 28 years (from the third to the thirty-first year); Béron (case 2), 34 years, and Balina, Braceras and Kaminsky (from puberty to the thirty-third year). A sharp division of types, however, should not be based on age. In several cases malignant acanthosis nigricans has started at birth or in early childhood or shortly after puberty (table 2).

2. The duration of the cutaneous disease should be noted. We know that it is common to see acanthosis nigricans precede cancer by several months. But even a long freedom from cancer—the longest period on record is eighteen years in Freund's case—is no guarantee against association with it.

3. The distribution of the cutaneous disease is of importance. Malignant acanthosis nigricans occurs mostly in symmetric distribution. So does benign acanthosis nigricans, however, in the majority of cases. Unilateral distribution of acanthosis nigricans would be indicative of the neviform character of the disease, but would not completely rule out the later possibility of an associated cancer

9. Although Hissard and Périn, who discussed the case, did not make a definite diagnosis of cancer, symptoms suggestive of gastric carcinoma were already marked before onset of the changes in the skin.

(Halty, Correa Delgado and Volpé and Becker). Gougerot, Blum and Eliascheff's patient may have shown the extreme beginnings of acanthosis nigricans. In a 34 year old woman acanthosis nigricans of only the left axilla was accidentally found. An internal cancer was not discovered.

4. All reported familial cases of acanthosis nigricans have so far been of the benign type (Tolmach: son, mother, two maternal uncles and maternal grandfather; Kémeri: father, three daughters, one son; Sandbacka-Holmström: mother, two daughters; P. J. Schwarz: father and one sister with suspicious, one brother with definite, lesions; Barnhardt: three generations of a family; W. Jadassohn: mother and two children; Miescher (1921) and Hellerström (1933): father, one son, one daughter; Buri: two brothers; Lange-Cosack: acanthosis nigricans together with chondrodystrophia in two (not all) children, father and grandfather; Bloch: brother and sister).

5. The behavior of the skin appears to be a very important clue to the character of the disease. Spreading of the cutaneous lesions, if it does not occur at onset in childhood or at puberty, seems to be an ominous sign indicating the presence of cancer. The fact that in many cases cancer and acanthosis nigricans spread simultaneously would permit the conclusion that spreading of the cutaneous lesions is a bad prognostic sign in malignant acanthosis nigricans, even if the tumor still seems to be checked by therapy or if the case has heretofore been considered one of benign acanthosis nigricans.

6. The general condition of the patient should be studied most carefully. In the presence of acanthosis nigricans loss of weight, abdominal pain, jaundice, gastric anacidity, enlargement of the liver and edema have serious significance and deserve the greatest attention. Many of the cases reported as instances of benign acanthosis nigricans in the literature have not been observed long and thoroughly enough. A few notes have been published, in which authors who originally reported their cases as benign stated that their patients had later become ill with cancer or had died (Grace and Schwartz; Little; Burgess [in discussion on Dowling and Freudenthal]; Arndt [in discussion on Spietschka, 3]; Périn [in discussion on Hissard]). McDonald's patient with metastases, whose relatively good general condition was expressly noted, died shortly after the presentation (personal communication to the author).

CONCLUSIONS

Cancers associated with acanthosis nigricans possess no unique or remarkably new features. Analysis and comparison reveal the evident homology of their qualities. The cancers occur in various organs, are usually of the glandular type and are highly malignant. The preponderance of gastric cancer among the cancers associated with acanthosis nigricans corresponds to its high general incidence.

SUMMARY

A cancer of the breast in a woman with acanthosis nigricans proved to be highly malignant, like other cancers that have been associated with acanthosis nigricans. Benign and malignant acanthosis nigricans are identical. Previous concepts of the causation of acanthosis nigricans, such as those attributing it to disturbances of the sympathetic nervous system or of the adrenals or other endocrine glands, should be discounted and cancer considered the essential etiologic factor of acanthosis nigricans. In cases of malignant acanthosis nigricans some properties of the tumor may activate the cutaneous lesions. In the benign type the same role of activation seems to be played by one of the sex hormones. The

role of cancer in family histories of patients with acanthosis nigricans, the type of cancers that have been associated with acanthosis nigricans and the chronologic independence of acanthosis nigricans and cancer speak for a genetic relationship between acanthosis nigricans and cancer.

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SICKLE CELL DISEASE

WITH SPECIAL REGARD TO ITS NONANEMIC VARIETY

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Three years ago it was pointed out by one of us [1] that the disease known as sickle cell anemia might better be named sickle cell disease, because anemia, though the best known and most frequent sign of this disease, is not the essential and not the most dangerous one. If this fact is not realized, diagnostic mistakes with disastrous consequences may occur. It is assumed that circulatory stasis in the small blood vessels of the internal organs is the primary and the most perilous consequence of the sickle cell trait (sicklemia), which is an inborn and constitutional abnormality of the red blood corpuscles encountered so far almost exclusively in Negroes. Patients afflicted with this disease do not, as a rule, die from anemia but may die from circulatory stasis in some vital organs. Since the sickling phenomenon—that is, the distortion of the red blood corpuscles of the affected persons—is markedly enhanced, both in vitro and in vivo, by lack of oxygen and accumulation of carbon dioxide, any situation may become fateful that might bring about a diminution of oxygen supply. For this reason patients with sickle cell disease are poor medical and surgical risks. It is important to recognize this fact, as the disease is frequently not diagnosed, and patients are operated on unnecessarily because an erroneous diagnosis of appendicitis, gallbladder disease or some other type of acute abdominal disease has been made.

It has been estimated that about 7.5 per cent of North American Negroes exhibit the constitutional sickle cell trait. Even if this estimate is somewhat exaggerated, as we are inclined to believe, it is evident that the potential danger involved is by no means negligible, particularly as far as our armed forces are concerned. It has been demanded [1] that all Negro patients in both medical and surgical services be tested routinely for sicklemia. By this simple procedure many erroneous diagnoses could be avoided, such as rheumatic fever, rheumatic heart disease, polyarthritis, osteomyelitis, typhoid and other infectious diseases, cerebral disease, peptic ulcer, appendicitis and cholecystitis.[2] "It is particularly important that patients in surgical services should be so tested and that a positive result be regarded as calling for a revision of the indications for the proposed operation. Surgical treatment should not be given until the measures outlined have been instituted and carried out." [1] Those measures aim at counteracting anoxemia and circulatory stasis. Routine testing for sicklemia is being done according to this

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1. Bauer, J.: Sickle Cell Disease, Arch. Surg. **41**:1344 (Dec.) 1940.

2. Diggs, L. W., and Bibb, J.: The Erythrocyte in Sickle Cell Anemia, J. A. M. A. **112**:695 (Feb. 25) 1939.

demand in the surgical department of Louisiana State University. For obvious reasons this practice should be carried on in the armed forces.

The present paper aims at supporting this demand. It will illustrate (1) that many cases of sickle cell disease are not diagnosed, and not even suspected, (2) that anemia is not necessarily present in patients with sickle cell disease, (3) that the cause of death may remain undetermined even at autopsy if the true nature of sickle cell disease is not given due consideration and (4) that persons with sickle cell disease represent biologic liabilities.

Since 1935 at the Los Angeles County General Hospital 6 patients have come to autopsy in whom "sickle cell anemia" was diagnosed by the pathologist. For 5 of these this diagnosis had not even been suspected by the clinicians. A similar experience has been reported by Wertham, Mitchell and Angrist.[3] In 4 of their 5 cases the diagnosis was made only post mortem, by examination of the organs and blood.

REPORT OF CASES

CASE 1.[4]—James W., a 24 year old Negro, was admitted to the hospital on March 6, 1936. All his life the patient had had vague pains in the joints and bones which came on suddenly and disappeared spontaneously. He was first admitted to the hospital in 1928 complaining of pain in the right leg and in the jaw. Syphilitic periostitis was diagnosed, but the Wassermann reaction proved to be negative. In 1930 the patient was hospitalized because of dull, aching pain in the left hip. Roentgenograms showed changes suggestive of Perthes' disease or of tuberculosis of the hip joint but characteristic of neither. A series of roentgenograms taken throughout the various periods at the hospital were inconclusive. They showed a "local area of cystic degeneration, cause undetermined." The blood count in 1930 was as follows: red blood cells 5,150,000, white blood cells 6,500 and polymorphonuclear neutrophils 78 per cent. The smear was reported to be normal.

In the succeeding years the patient was admitted to the hospital twice for acute abdominal complaints. Both times he refused operation and recovered spontaneously.

On Aug. 15, 1933, a biopsy of the left hip was done. It showed macroscopically "marked thickening of synovia and a small amount of caseous-like material, giving evidence grossly of tuberculosis." This, however, was disproved by the microscopic study: "Sections show extensive fibrosis, areas of chronic inflammatory reaction with no evidence of tuberculosis. Some areas show many plasma cells."

On Aug. 30, 1935, the patient suddenly became ill with sharp pain in the epigastrium, followed by severe and continuous generalized abdominal pain. He vomited several times. Diagnosis of possible ruptured ulcer was made, but the patient refused an operation and recovered after several days. At this time the hemoglobin was found to be 90 per cent, the white blood cells 8,100 and the polymorphonuclears 76 per cent.

The last admission was for pneumonia, which was fatal two weeks after onset.

Autopsy.—Autopsy was performed on March 9, 1936, by Dr. J. P. Fitzgibbon. The patient was a well developed and well nourished Negro man. There was a scar, apparently of an old ulcer, over the anterior surface of the left leg near the ankle and a healed surgical scar over the left hip. On the epicardial surface there were fine splinter-like petechial hemorrhages. The myocardium was somewhat flabby and light brownish red. The aorta was normal. Pneumonia of the right lower lobe was apparent. The digestive system appeared normal. Particularly there was no evidence of the existence, past or present, of peptic ulcer. The liver weighed 1,700 Gm. and was dark purplish maroon. The spleen weighed 550 Gm. Several infarctions were to be seen. The lymphoid tissue of the mesentery was hyperplastic. The urinary and genital tracts were essentially normal. The adrenals were small and firm and appeared essentially normal.

The head of the femur appeared to have been destroyed by processes of roughening of the articular surface. The neck of the femur showed alternate areas of bone destruction and proliferation with osteophytes. The shaft of the femur itself at its cross section showed considerable cortical thickening and extreme narrowing of the marrow cavity, so that there was

3. Wertham, F.; Mitchell, N., and Angrist, A.: Brain in Sickle Cell Anemia, Arch. Neurol. & Psychiat. **47**:752 (May) 1942.

4. This case, which is included by permission, is to be published in more extended form as a separate report by Drs. J. P. Fitzgibbon and R. A. Carter.

only a thin line of light brown marrow substance left. The sternum was followed across and the marrow appeared light brownish red and was essentially normal.

Microscopic Examination.—The fibers of the heart appeared of normal size. Under low power increased cellularity was especially pronounced around all the small vessels. There were no large scars. Definite sickled cells were in the capillaries. The alveolar walls of the lungs were not easily identified, but the alveolar spaces were crowded with polymorphonuclears and some macrophages and fibrin. The bronchial epithelium was normal. Another section showed alternating areas of alveoli filled with polymorphonuclears, macrophages and areas of necrosis in which the remains of alveolar structure could usually be seen. The vessels in these parts of the section particularly were packed with oat-shaped cells. The central areas of the liver were packed with oat-shaped and sickle cells, as were the sinusoids. The hepatic cells themselves were fairly intact. The triads contained some extra round cells and a large number of cells of the myeloid series, mostly polymorphonuclear, and there were a few collections of these cells in the lobules themselves. About half of the section of the spleen showed fairly normal-appearing malpighian bodies in the pulp, which was intensely packed with abnormal red cells, although the normal splenic structure was destroyed. The rest of the section was pale and made up of fibroblasts scattered in a background of broken-down red cells. The vessels were packed with sickle cells and fibrin. The line of demarcation was sharp. In the kidney glomerular tufts were congested here and there with red blood cells, as were the vessels in the region of the convoluted tubules, which were normal. The vessel walls were not remarkable. There were no inflammatory foci. The glomerular centers were hyperplastic, and the vessels were congested. There was considerable replacement in one part of the connective tissue, possibly due to an old infarction. Two sections of bone showed trabeculations of the cortex extending entirely through the medulla to the other surface of the cortex. The medullary tissue was enclosed in islands between the bone trabeculae. There were excessive numbers of myeloid series in all stages of development in the medulla.

The anatomic diagnosis was sickle cell anemia, lobar pneumonia of the right lower lobe, splenomegaly with infarctions and osteosclerosis of the left femur, with destruction of the left hip joint.

Comment.—This case is instructive for the following reasons: The history and course of sickle cell disease are typical as far as pain in the bones and joints and acute abdominal crises are concerned. Anemia, however, was absent at a time when marked structural changes of the skeleton were evident and an acute abdominal crisis occurred. The changes in the bones could not be interpreted because the sickling phenomenon had not been looked for. The correct interpretation of the roentgenograms was not possible before the autopsy and particularly before the microscopic examination had revealed the characteristics of sickle cell disease. The term sickle cell anemia is not justified in such a case because pathologic changes due to sickle cell disease were present when anemia did not exist, and because even at autopsy no indication of anemia was found. The dark purplish maroon color of the liver is not in accord with anemia. Splenomegaly with infarcts, hyperplastic lymph nodes in the mesentery, the changes of the skeleton and the engorgement with distorted red blood corpuscles of the vessels of the lung, liver and spleen proved the case to be one of sickle cell disease apparently without anemia. Sicklemia had caused a serious disease but not anemia.

Case 2.—Eloise A., a 26 year old Negress, was admitted to the hospital on July 24, 1935, complaining of severe pain in the back on both sides, particularly on the left, chills, fever and vomiting for four hours. Her past history and family history were irrelevant. The patient was well developed and well nourished. Her temperature was 98.2 F., the pulse rate 96 and the respiratory rate 44. There were no abnormalities in the lungs or heart. There was generalized rigidity of the abdomen, most marked in the left lower quadrant, and extreme tenderness of the whole abdomen. The patient had stiffness of the neck and generalized muscular tenderness, especially of the muscles of the extremities. The urine contained traces of albumin but no sugar. There were 10 white blood cells per high power field. The Gram stain showed numerous gram-negative rods but few gram-positive cocci. The white blood cell count was 9,500, polymorphonuclears 86 per cent and lymphocytes 14 per cent, and non-protein nitrogen 16 mg. per hundred cubic centimeters. Phenolsulfonphthalein appeared in the urine in four minutes—45 per cent in one-half hour, 15 per cent in one hour. Roentgeno-

grams of the kidneys, ureters and bladder indicated normal conditions. The patient died after three days of severe pain. A clinical diagnosis was not made.

Autopsy.—Autopsy was performed on July 27 by Dr. L. J. Tragerman. The skull and central nervous system, heart and aorta, respiratory system and digestive system were essentially normal, except for moderate congestion of the lower lobes of the lungs. The liver weighed 1,590 Gm., was mottled, mahogany brown and of slightly softer than average consistency. The cut surfaces were reddish brown. The spleen was greatly enlarged, weighed 620 Gm. and was dark reddish brown. The cut surfaces were dark mahogany brown and moderately firm. Malpighian markings were totally obscured. There was no enlargement of cervical, axillary and inguinal lymph nodes. The left kidney weighed 170 Gm.; the capsule stripped easily from a smooth, lightly ecchymotic, brown surface; there were three small areas of old infarction visible on external examination. The cut surface was apparently normal, except for many punctate hemorrhages throughout. The right kidney weighed 165 Gm.; the capsule stripped easily from a smooth, brown surface, and surfaces of the sections were apparently normal. Pelves and ureters were normal. The urinary bladder was normal, except for slight ecchymoses in the region of the trigone. There was marked hyperemia of the uterus, tubes and ovaries. The adrenals were apparently normal. The skeletal system also was apparently normal.

Microscopic examination of sections of the liver and kidneys showed sickling of the red blood cells: cloudy swelling, tubular degeneration, acute glomerulitis and infarctions of the kidneys; cloudy swelling of the liver with periportal infiltration (round cells and polymorphonuclears); hemorrhagic splenomegaly, and pulmonary edema.

The anatomic diagnosis was hemorrhagic splenomegaly, punctate hemorrhages of the kidneys and sickle cell anemia.

The probable and official cause of death was not determined by autopsy (Dr. O. M. Stewart).

Comment.—Anemia, particularly sickle cell anemia, had not been suspected clinically, and therefore a red cell count had not been done. Even at autopsy there was no evidence of anemia. Yet the hemorrhagic splenomegaly and the microscopic evidence of sickled erythrocytes were proof of sickle cell disease. The important fact is that the pathologist was unable to determine the cause of death and to explain the clinical symptoms. Rightly he did not consider the pathologic changes of the kidneys a causal factor of death. Clinically there was no evidence of renal functional failure. As long as the true nature of the disease—that is, the vascular engorgement with disfigured erythrocytes resulting in circulatory stasis—had not been recognized, both the clinical picture and the cause of death must have remained mysterious. Whether or not such a circulatory stasis could have been found in the small vessels of the splanchnic area and of various muscles cannot be established, as it had not been looked for. Yet we venture to guess that circulatory stasis was present, because such a finding would be in accord with our conception of sickle cell disease and would explain the acute abdominal symptoms, the stiffness of the neck, the muscular tenderness and the eventual death.

Case 3.—Margret M., an 80 year old Negress, was admitted to the hospital on Aug. 16, 1935, one week before her death. She was too enfeebled and later too stuporous to give a history. She was incontinent of urine and feces and had a large sacral decubital ulcer. Physical examination gave essentially normal results. The blood pressure was 140 systolic and 85 diastolic, nonprotein nitrogen 60 mg. and creatinine 1.6 mg. per hundred cubic centimeters. No blood count was done. The clinical diagnosis was generalized arteriosclerosis.

Autopsy.—Autopsy was performed on Aug. 26, 1935 by Dr. E. J. Joergenson. The following changes were revealed: greatly atheromatous and tortuous arteries at the base of the brain, some hydrocephalus and slight atheromatosis of the aorta and of the coronary arteries. The heart, lungs and digestive tract were essentially normal except for old pleural and peritoneal adhesions. The liver was brownish black on the cut surface. The spleen was atrophic and fibrous, and its weight was only 25 Gm. The lymphoid tissue of the periaortic lymph nodes appeared to be somewhat increased. The urinary system was normal, and the kidneys had a smooth brown surface. The bone marrow of ribs and vertebrae appeared red.

Mounts of the venous blood revealed definite sickling after standing for several hours.

Microscopic examination of the spleen showed marked hyalinization of the capsule and septums. The malpighian arteries were mostly obliterated. There were oat-shaped red blood corpuscles in the pulp.

The official cause of death was declared to be sickle cell anemia (Dr. C. H. Francis).

Comment.—Again anemia had not been suspected, and therefore a blood count had not been done. Anemia was not proved at autopsy either, as can be concluded from the color of the liver and kidneys. Death was sufficiently explained by the arteriosclerosis. The patient had, however, sickle cell disease with the characteristic changes of the spleen, the hyperplastic abdominal lymph nodes and the red bone marrow. This case illustrates the known fact that persons with sickle cell disease may occasionally escape the hazards of their unfortunate constitution and reach old age.

CASE 4.—Leah S., a 20 year old Negress, was admitted to the hospital on April 22, 1935. She was in the fifth month of pregnancy and entered the hospital because of dyspnea, pain in the chest and cough with raising of blood-tinged sputum for four weeks. Her temperature was 101 F. and her pulse rate 120. The scleras were icteric. Dulness, decreased breath sounds and crepitant rales with increased tactile fremitus over both lower lobes of the lungs were found. The heart was normal and the blood pressure 115 systolic and 70 diastolic. The uterus was enlarged. The liver and spleen were not palpable.

The urine was negative for albumin and sugar. The red blood cell count was 1,920,000, hemoglobin 35 per cent, color index 0.92, white blood cells 26,000, polymorphonuclears 87.5 per cent, monocytes 9 per cent and lymphocytes 3.5 per cent. The red cells were predominantly large and relatively hypochromic. The platelets appeared normal.

The clinical diagnosis was bilateral bronchopneumonia and macrocytic anemia of pregnancy.

Autopsy.—Autopsy was performed by Dr. L. J. Tragerman on April 22, 1935. Multiple infarcts in the lower lobes of both lungs were due to embolisms originating from thrombophlebitis of the uterine veins. The body of the uterus was symmetrically enlarged, and its cavity was filled with normal attached placenta and an amniotic sac containing well developed twins about 20 cm. in length. The cut surface of the liver was pale brown with normal markings. The spleen was unusually small, measuring about 3 cm. in length, weighing less than 25 Gm. and containing an old infarct. The bone marrow in the lower end of the femur and in the middle of the tibia was bright red.

The official cause of death was declared to be pelvic thrombophlebitis with multiple pulmonary infarcts and macrocytic anemia of pregnancy (Dr. H. B. Haining).

Microscopic section of the spleen showed sickle cells in the reticulum and severe siderofibrosis.

Comment.—This case does not require particular comment. There were anemia and pregnancy. Yet, whether the anemia did not exist before the pregnancy was not known. In spite of the icteric scleras, the sickling phenomenon had not been looked for. Whether the case should be classified as macrocytic anemia of pregnancy or as sickle cell anemia with pregnancy cannot be decided. That not only sicklemia but sickle cell disease had been present was proved by the characteristic appearance of the spleen.

CASE 5.—Laura M. de H., a 14 year old Negress, was admitted to the hospital on August 21, 1940 in coma and died thirty minutes after admission, in spite of emergency treatment. The only available information concerned her severe vaginal bleeding for the past month. Two similar episodes had occurred in the past four years. The patient was extremely pale. Her respiration was gasping and stertorous, and the rate was 15 per minute. No radial pulse was palpable. The apical rate was 80 and the rhythm was regular. There were moist rales at the bases of both lungs. Pelvic examination revealed the hymenal ring intact and the cervix closed and firm, with oozing of a moderate amount of serosanguineous fluid. The corpus uteri was of average size, at the left and anteriorly. The adnexa were normal.

Autopsy.—Autopsy was performed on August 21 by Dr. S. D. Leo. The body was that of a well developed and well nourished, somewhat obese mature Negress weighing 72.5 Kg. and measuring 150 cm. in length. There was excessive hair on the side of the face and over the entire mid-region of the back. No icterus was present, but there was pronounced pallor of all visible mucous membranes. The breasts were well developed, with a large amount of glandular tissue. There were striae distensae over the thighs and breasts. No

gross abnormalities were observed of the skull, central nervous system or cardiovascular system except for extreme anemia. The level of the right side of the diaphragm was at the third rib, that of the left side at the third interspace. Each lung weighed 250 Gm. The thymus appeared pale and weighed 46 Gm. after removal of the parathymic fat. Otherwise the organs of the chest, the digestive and hepatic system, spleen and lymphatic system and urinary tract displayed no gross abnormality except anemia. Neither was there any gross abnormality of the thyroid, parathyroids, adrenals and pituitary gland. The bone marrow of the sternum and of the skull appeared extremely anemic. The uterus was about one and one-half times normal size, and the endometrium was definitely hyperplastic and cheeselike in consistency, with blood-tinged areas and blood clots. The ovaries were about two and one-half times normal size and rather soft. The color of the external part was white with a tinge of blue. The cut surfaces of both ovaries revealed numerous small follicular cysts, none larger than 3 mm. in diameter. In addition, the left ovary contained a large cyst, about the size of a small grape, which was filled with red fluid blood.

Postmortem examination of the blood revealed: hemoglobin 1.2 Gm. (7.4 per cent), red blood cells 320,000, color index 0.82, white blood cells 21,600, a reduced number of platelets, polymorphonuclears 36.5 per cent, lymphocytes 58 per cent, mononuclears 1.5 per cent, metamyelocytes 1.5 per cent, myelocytes 2.5 per cent and 11 normoblasts per 200 white blood cells. Sickle cell preparation showed typical sickling of red cells. The Wassermann reaction was negative.

Microscopic examination showed great endometrial hyperplasia in the proliferative phase with hemorrhages; multiple maturing ovarian follicles in all stages of development and numerous follicular cysts but no corpus luteum formation, and hyperplasia of red and white elements of the bone marrow. In the spleen there were areas of hemorrhage around some small malpighian follicles. The capsule and trabeculae were normal. Many deformed erythrocytes, some sickle shaped, were found in the spleen and liver.

The official cause of death was declared to be endometrial hyperplasia with hemorrhage and sickle cell anemia (Dr. Gertrude Finkelstein).

Comment.—This case is of interest for the following reasons. There is no proof of sickle cell anemia, and scarcely of sickle cell disease. The fatal anemia resulted from the uterine hemorrhage, and this was due to the follicular cystic degeneration of the ovaries with failure of corpus luteum production. It was a typical case of fatal postpubertal hemorrhage. The absence of icterus is not in accord with sickle cell anemia. The anemia was obviously posthemorrhagic, not hemolytic, in nature. The microscopic changes in the spleen might suggest the very first stage of circulatory stasis due to a beginning of sickle cell disease.

The combination of the sickle cell trait (sicklemia) with the cystic degeneration of the ovary, however, deserves attention. The sickle cell trait is a constitutional abnormality that may or may not result in a serious disease. It is indicative of at least one abnormal gene representing a definite morbid predisposition (to sickle cell disease). As has been pointed out elsewhere,[5] it is to be expected that not infrequently this abnormal gene is only one among many other pathologic genes; in other words, that sicklemia is one of numerous constitutional deviations of a person from the normal average. In the paper just quoted,[1] several examples were reported of such a multiple genotypic deviation called "status degenerativus," including, among others, the sickle cell trait. It is important to recognize that the well defined genopathy predisposing to sickle cell disease may be indicative of farther reaching chromosomal abnormalities known as status degenerativus.

In our case such a status degenerativus is evident from the following findings proving or suggesting constitutional (genotypic) abnormalities: cystic degeneration of the ovaries, hyperplastic thymus weighing 46 Gm., the abnormally high level of the diaphragm, lymphocytosis of 58 per cent among 21,600 white blood cells, hypertrichosis and mild obesity. That the diaphragm may be found at a higher level in persons with status thymolymphaticus was emphasized by Byloff[6]

5. Bauer, J.: Constitution and Disease: Applied Constitutional Pathology, New York, Grune & Stratton, Inc., 1942; footnote 1.

6. Byloff, K., cited by Bauer.[7]

in 1914. It is, however, nothing but a degenerative stigma mostly associated with other genopathies.[7]

CASE 6.—Jennie H., a 33 year old Negress, was admitted to the hospital April 16, 1940. She was first seen in the internal medicine clinic in October, 1936. She complained of weakness during the preceding six months and of shortness of breath on exertion for several years. Her last menstruation was in 1933. Diagnosis of sickle cell anemia was made. The red blood cell count was 3,480,000, hemoglobin 54 per cent, color index 0.79, white blood cells 12,550, polymorphonuclears 48 per cent, lymphocytes 48 per cent, eosinophils 3 per cent and monocytes 1 per cent. There were pronounced poikilocytosis, anisocytosis and sicklemia. The patient was treated with liver extract but responded only slightly. By December 1937, her hemoglobin had risen from 54 per cent to 84 per cent. She was admitted to the hospital on Jan. 9, 1938, with symptoms of an acute abdominal condition and recovered without surgical intervention. One blood transfusion was tolerated without reaction. She was discharged on January 22. Liver therapy was continued, but the patient was readmitted on June 21 and October 10, and again on April 16, 1940, because of increasing anemia. Several transfusions were given each time. One severe reaction occurred in June 1938. On May 1, 1940, the hemoglobin was 50 per cent and the red blood cells 2,710,000 with marked sickling. Another direct transfusion was done. The next day the patient had a temperature of 102 F., albuminuria and severe backache. She died two days after the transfusion. The physical examination was reported as giving essentially normal results except for the icteric tinge of the scleras and a systolic murmur at the apex of the heart. The urine was normal and the Wassermann reaction negative.

Autopsy.—Autopsy was performed on May 3 by Dr. B. E. Levine. There was an extensive subdural hemorrhage covering the major portion of the dorsolateral surface of the right cerebral hemsiphere which evidently had caused the death of the patient. The aorta showed minimal subintimal cholesterol deposits. There was pulmonary edema. The gallbladder contained four irregular pigmented stones, the largest of which measured 4 mm. in diameter. The spleen was found with difficulty and was extremely atrophic. It weighed 2.5 Gm. and measured 3 by 1 by 0.4 cm. There was a generalized enlargement of the lymph nodes, including the tracheobronchial, abdominal and even epitrochlear. The lymph follicles of the stomach and the solitary follicles of the intestines were hyperplastic. The thymus was greatly enlarged and weighed 65 Gm., and it had little perithymic fat. The bone marrow of the sternum, vertebrae and femur appeared red and hyperplastic. Pubic hair was somewhat scanty. In the right anterior axillary line overlying the costal margin was an irregular, ovoid dark brown birthmark measuring 4.5 by 3.5 cm. The circumference of the pulmonary artery was 8 cm., that of the aorta 6.5 cm. The left lung presented an anomaly in that only a single lobe was demonstrable. Within the cortex of the left kidney was a smooth-walled cyst 1 cm. in diameter. The uterus, tubes and ovaries as well as the thyroid, pituitary and adrenals appeared to be normal.

Microscopic examination showed the typical hemosiderotic, hyalinized, fibrous spleen with only a few areas of lymphocytes and congested vessels. The sinusoids of the liver were greatly dilated and filled with bizarre-shaped red blood cells. The hepatic cords were thinned and atrophic, many cells showing cloudy swelling. Extreme vascular congestion with oat-shaped and sickled erythrocytes was found in the kidneys, pancreas, lungs and pituitary. Tubular necrosis and hemosiderosis of the kidneys were apparent.

The official cause of death was declared to be massive subdural hemorrhage after blood transfusion and sickle cell anemia (Dr. R. M. Hill).

Comment.—Among the 6 reported, this was the only case in which the diagnosis sickle cell anemia had been made clinically. The clinical picture and course as well as the underlying pathologic changes observed at autopsy were typical. Severe reactions and even death of a patient with sickle cell disease after a blood transfusion have been reported previously.[8] Such a reaction may occur even if previous transfusions have been well tolerated.

This case again illustrates a status degenerativus: status thymicus, the abnormality of the left lung, the amenorrhea and scanty pubic hair, the birthmark, the

7. Bauer, J.: Konstitutionelle Disposition zu inneren Krankheiten, ed. 3, Berlin, Julius Springer, 1924.

8. (*a*) Tomlinson, W. J.: Studies of Sicklemia Blood, Am. J. Clin. Path. **11**:835 (Nov.) 1941. (*b*) Wintrobe, M. M.: Clinical Hematology, Philadelphia, Lea & Febiger, 1942. (*c*) Bauer.[1]

lymphocytosis of 48 per cent among 12,550 white blood cells and the relative preponderance of the pulmonary artery as compared with the width of the aorta may be considered as signs of an abnormal constitution. The generalized hyperplasia of the lymphatic tissue is frequent in sickle cell disease [1] and probably a direct consequence of the disease rather than a constitutional stigma. Gallstones and solitary cysts in the kidneys are too frequent to permit of any evaluation in our case.

CASE 7.—Finally the history of a case may be referred to which fortunately did not come to autopsy but which nevertheless illustrates several essential facts: (1) that a person of white race without known Negro ancestry may be subject to sickle cell disease; (2) that sickle cell disease may not be suspected in a patient presenting the clinical picture of an acute abdominal condition, and (3) that a severe condition may result from sickle cell disease without marked anemia.

The history of this case will be reported extensively by Drs. Canby, Carpenter and Ellmore from Southern California University Medical School.

It is the case of a 19 year old white youth born of Sicilian parents who was operated on when a diagnosis of torsion of the spleen on its pedicle was made. Splenomegaly of a considerable degree was found with an extensive area of fibrinous perisplenitis. There was no torsion of the spleen or gross evidence of splenic vein thrombosis, and the liver appeared to be normal. Splenectomy was done.

After the operation marked sickling of the red blood cells was found, and the microscopic examination of the spleen revealed the typical picture of sickle cell disease. There was practically no anemia, but the icterus index was found to be 44.

Comment.—There exist only a few reports of sickle cell anemia in persons of the white race. According to Wintrobe [8b] there are now reports of 7 instances of sickle cell anemia in white families which seem unchallengeable. Lewis [9] recognizes only 3 instances in pure Caucasians and considers even these as questionable because of the possibility of admixture of Negro blood in past generations. This view is shared by Ogden.[10] In fact, almost all the cases of sickle cell anemia observed in persons of the white race were in patients of Greek, Italian or Sicilian stock. Two more cases in white children of southern Italian descent were reported recently.[11] The patient in case 7, too, was born of Sicilian parents. We agree with Morrison, Samwick and Landsberg [11] that search for the sickling phenomenon should be undertaken in all cases of obscure hemolytic disorders, even in white patients. The case to be reported by Canby, Carpenter and Ellmore, however, demonstrates that such a search should not be limited to patients with obvious anemia of hemolytic origin. This patient had only a negligible reduction of hemoglobin (12 Gm., 75 per cent) and a normal red cell count (4,750,000). Yet the icterus index was increased (44). Sickle cell disease without anemia may, therefore, occur also in persons of the white race and may cause a serious clinical picture. The clinical picture presented by this patient is the only possibly justified indication for splenectomy in sickle cell disease. The acute development of an extremely painful splenomegaly aroused the suspicion of a torsion of the spleen on its pedicle or of a thrombosis of the splenic vein. It can be assumed, however, that the patient would have recovered even without the operation.

The fact that the patient's parents and siblings did not have the sickle cell trait is at variance with the assumption that sicklemia is transmitted by heredity as a simple dominant mendelian characteristic. It can hardly be surmised that the sickle cell trait of our patient was caused by mutation, since the occurrence of this trait in the white race is questionable.

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9. Lewis, J. H.: Biology of the Negro, Chicago, University of Chicago Press, 1942.

10. Ogden, M. A.: Sickle Cell Anemia in the White Race, with Report of Cases in Two Families, Arch. Int. Med. **71**:164 (Feb.) 1943.

11. Morrison, M.; Samwick, A. A., and Landsberg, E.: Sickle Cell Anemia in the White Race, Am. J. Dis. Child. **64**:881 (Nov.) 1942.

COMMENT

When the material presented here is considered, reason dictates that to abandon the misnomer sickle cell anemia and to use the term sickle cell disease [1] is not only justified but imperative. Anemia is only one of the consequences and the most frequent and obvious sign of this disease. One does not call a cancer or a peptic ulcer resulting in anemia cancer-anemia or ulcer-anemia but designates it as cancer or ulcer with subsequent anemia. The question is not only one of academic terminology but also the highly practical one of the correct conception of the underlying pathologic anatomy and physiology. It is essential to have this conception in order to avoid erroneous diagnoses and treatments and to institute correct management. The main danger to the patient does not result from the anemia—this has also been emphasized by W. Schiller [12]—but from the circulatory stasis in various organs. Cases 1 and 7 prove that a serious impairment of health may occur in sickle cell disease without anemia.

We cannot agree with Wintrobe [8b] when he considers the sickle cell trait "to be of little clinical significance" (p. 467) and when he says that "in association with the trait alone, neither anemia nor the above symptoms [i. e., symptoms suggesting acute abdominal disease, rheumatic fever, osteomyelitis or neurologic disorders] are produced." Our observations are not in accord with Wintrobe's claim that for the diagnosis of such a case sickling of the red blood cells is not sufficient but that sicklemia, anemia with active red cell regeneration, leukocytosis and bilirubinemia are necessary (p. 464). We subscribe, however, to his somewhat contradictory statement that "the difference between sickle cell anemia and the sickle cell trait may perhaps be only one of degree" (p. 467).

A person burdened with the constitutional sickle cell trait has one of the following chances:

1. He may have the constitutional sickle cell trait without any further consequences.

2. There may develop an actual sickle cell disease, as proved by the characteristic anatomic findings, chiefly in the spleen, but without noticeable impairment of health. Such a condition is not incompatible with the attainment of old age (case 3).

3. Actual sickle cell disease may develop, causing circulatory stasis in various organs and thereby producing abdominal or neurologic symptoms, pain of bones and joints and other manifestations of such an impaired circulation. Anemia is not a necessary sign, as demonstrated by cases 1 and 7.

4. A more or less severe anemia may develop as the leading sign of sickle cell disease. This is the full-fledged sickle cell anemia (case 6).

5. The sickle cell trait may be present and the patient may be on the verge of sickle cell disease or have an actual sickle cell disease but suffer from severe anemia of a nature different from sickle cell anemia (cases 4 and 5).

6. Having the sickle cell trait, whether or not resulting in sickle cell disease with or without anemia, he may become the victim of his constitutional biologic inferiority and succumb under circumstances which are innocuous to average normal people. The condition may be due to one of two factors:

(*a*) The mechanism which facilitates the conversion of sicklemia into sickle cell disease or accelerates the progress of sickle cell disease may be set into action if a large number of red corpuscles are caused to sickle. This may be brought about by local or general anoxemia, which in turn may result from infectious

12. Schiller, W., in discussion on Kobak, Stein and Daro,[13] p. 821.

diseases, surgical procedures and other circumstances that are known to slow the circulation of the blood. Pregnancy also may be such a factor.[13] The risk of blood transfusions has been mentioned.[8]

(*b*) Persons with the sickle cell trait may also have other constitutional abnormalities. In other words, they may be representatives of a "status degenerativus."[14] Such a constitutional state has to be considered as a biologic liability, lowering the resistance and adaptive power. Our cases 5 and 6, as some other cases of sickle cell disease previously reported by one of us (J. B.),[1] are instances of a status degenerativus. We find a confirmation of our view by Wintrobe[8b]: "Sickling of the red corpuscles may therefore be only one of several degenerative stigmas with which these individuals are burdened" (p. 467). Wintrobe reports the case of a 22 year old Negro with sickle cell anemia showing tower skull. He appeared younger than his stated age and was found to have bilateral hypoplasia of the terminal phalanx of the fourth finger, a funnel chest, spina bifida, bilateral saber deformity of the tibia and hallux valgus.

The anemia resulting from sickle cell disease is hemolytic in nature. The pathogenesis has been obscure. In 1940 one of us (J. B.)[1] advanced the theory that the anemia is caused by the deterioration of masses of deformed red blood corpuscles which are impacted in the smaller blood vessels of various organs, chiefly in the spleen and liver. Stagnation and conglutination of the red cells, such as are seen in cases of sickle cell anemia, must eventually lead to disintegration of the corpuscles without regard to whether or not an actual thrombosis did develop. The disintegration of the conglutinated erythrocytes sets free hemoglobin which is transformed into the hematogenous pigment found in various organs and into bilirubin found in increased amounts in the blood serum.

We have been interested in seeking for some other pathologic state associated with circulatory stasis in small blood vessels in order to study the effect of such a stasis with regard to the clinical symptomatology and particularly with regard to the occurrence of a hemolytic anemia. Such an analogous morbid state was found in a rare disease described first by Moschcowitz,[15] later by Baehr, Klemperer and Schifrin,[16] and Gitlow and Goldmark[17] and more recently by Altschule.[18] According to the last-named author, it is a "rare type of acute thrombocytopenic purpura: widespread formation of platelet thrombi in capillaries." The cause of those platelet thrombi is unknown, but the large masses of thrombocytes involved with the formation of thrombi probably account for the peripheral thrombocytopenia and subsequent purpura.[16] No attempt is made here to discuss the nature of this disease. We agree with Altschule, however, that "attempts to relate this syndrome to acute disseminated lupus erythematosus because of the purpura and the finding of vascular lesions are not valid." What matters here is the occurrence of generalized capillary and arteriolar thromboses, whatever their cause and pathogenesis may be.

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13. Kobak, A. J.; Stein, P. J., and Daro, A. F.: Sickle Cell Anemia in Pregnancy, Am. J. Obst. & Gynec. **41**:811 (May) 1941.

14. Footnotes 1, 4 and 6.

15. Moschcowitz, E.: An Acute Febrile Pleiochromic Anemia with Hyaline Thrombosis of the Terminal Arterioles and Capillaries, Arch. Int. Med. **36**:89 (July) 1925.

16. Baehr, G.; Klemperer, P., and Schifrin, A.: An Acute Febrile Anemia and Thrombocytopenic Purpura with Diffuse Platelet Thromboses of Capillaries and Arterioles, Tr. A. Am. Physicians **51**:43, 1936.

17. Gitlow, S., and Goldmark, C.: Generalized Capillary and Arteriolar Thrombosis, Ann. Int. Med. **13**:1046 (Dec.) 1939.

18. Altschule, M. D.: A Rare Type of Acute Thrombocytopenic Purpura: Widespread Formation of Platelet Thrombi in Capillaries, New England J. Med. **227**:477 (Sept. 24) 1942.

If our conception of sickle cell disease is correct, then similar consequences of a widespread thrombosis are to be expected as they are observed in sickle cell disease. In fact, anemia is such a consequence of both diseases. Moschcowitz [15] as well as Baehr, Klemperer and Schifrin [16] entitled their report "an acute febrile anemia." This anemia must also be hemolytic in nature because it is frequently associated with icterus and because the bone marrow was found to be normal or showed a slight tendency to hyperplasia. The fragility of the red cells, when they were tested, was also found to be normal. Polymorphonuclear leukocytosis occurs both in sickle cell disease and in this peculiar malady. It is particularly remarkable that generalized aches and pains, especially about the joints, that diffuse abdominal pain with vomiting and that cerebral symptoms have been observed in this disease. Brain symptoms, such as confusion, mumbling speech or facial weakness, may disappear completely after a few minutes.[18] At autopsy, increase in the number of lymphocytes in the periportal areas in the liver and slight hyalinization of the media of the splenic arteries have been found. Anemic infarcts of the spleen and abundant amounts of iron pigment in the pulp have also been reported.

It need not be emphasized that this rare malady and sickle cell disease have nothing in common as far as their causation and pathogenesis are concerned. Both diseases, however, are characterized by circulatory stasis caused by widespread obstruction of small blood vessels, though the mechanism of this obstruction may be different in each. We are fully aware of the inability of ruling out the possibility that the hemolytic anemia in the cases of thrombocytopenic purpura may be due to the same unknown factor which causes the formation of platelet thrombi and may, therefore, be of different nature than the hemolytic anemia in sickle cell disease. Yet the far reaching similarities between both diseases enumerated seem to be more than suggestive that the circulatory stasis occurring in both may account for most of the clinical symptoms and signs and particularly for the hemolytic anemia. Nature frequently supplies facts that are just as valuable for the basis of conclusions as animal experiments carried out in laboratories. One has only to recognize such facts, note them by proper clinical observation and make intelligent interpretation.

SUMMARY

The 7 cases reported demonstrate various consequences of the constitutional sickle cell trait.

Anemia is not an obligatory sign of sickle cell disease.

Serious consequences may result from the circulatory stasis in the small blood vessels rather than from the anemia.

Anemia in sickle cell disease is explained as a consequence of the deterioration of the conglutinated distorted red blood cells that cause the circulatory stasis.

Persons with the sickle cell trait are potential candidates for sickle cell disease with or without anemia. They are frequently representatives of a status degenerativus and are biologic liabilities.

Many cases of sickle cell disease are not diagnosed correctly because the sickling phenomenon is not looked for.

All Negro patients in both medical and surgical services should be tested routinely for sicklemia.

This demand is particularly made with regard to the armed forces.

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CUTIS GRAFTS; APPLICATION OF THE DERMATOME-FLAP METHOD

ITS USE IN A CASE OF RECURRENT INCISIONAL HERNIA

SAMUEL A. SWENSON JR., M.D.
AND
HENRY N. HARKINS, M.D.
DETROIT

REVIEW OF THE LITERATURE

The use of cutis grafts in the place of free fascial transplants has received scant attention from American writers. Until 1942, when Cannaday made his first report,[1] the use of cutis grafts in this country was limited almost exclusively to the field of plastic surgery, in which it is applied in the reconstruction of tissue defects.

In 1913, Loewe [2] reported the first cases in which cutis material was used as a buried graft, including repair of inguinal and umbilical hernia and tendon repair. Six cases were reported, and these are included as a matter of historical interest.

CASE 1.—Injury of extensor pollicis longus tendon. It was impossible to approximate the severed ends of the tendon, so cutis material was used to bridge the defect. The functional result was not satisfactory.

CASE 2.—Inguinal hernia. A piece of the cutis 7 cm. by 3 cm. was sutured over Hesselbach's triangle and a piece 5 cm. by 2.5 cm. over the canal. A postoperative hematoma was aspirated, and the wound healed with no recurrence of the hernia.

CASE 3.—Umbilical hernia and midline laparotomy incision. The wounds were connected and the entire wound covered with a cutis graft 10 cm. by 4 cm.

CASE 4.—Double inguinal hernia. The canals on both sides were covered with cutis 5 cm. by 2.5 cm.

CASE 5.—Bladder hernia, inguinal. A piece of cutis 6 cm. by 3 cm. was sutured over the transversalis fascia; then the muscles were united to Poupart's ligament over the graft.

CASE 6.—Castration through inguinal approach. A weak inguinal canal was covered with cutis graft. Infection and scrotal abscess occurred postoperatively.

Loewe, in describing the technic for removal of the graft, stated that the skin was removed in the manner of any full thickness graft. The epidermis was then abraded away by scraping, as one would scrape a carrot. This tissue was then sutured over the defect under tension.

Again, in 1929, Loewe [3] reviewed his use of cutis grafts in nearly a hundred patients, adding numerous new procedures, such as using cutis material as sutures in gastroenterostomy, the replacement of dura, nerve suturing, arthroplasty and gastropexy. He observed that these grafts heal in place and that epidermoid elements tend to degenerate. Most of his results were favorable.

From the Department of General Surgery, Henry Ford Hospital.

1. Cannaday, J. E.: The Use of the Cutis Graft in the Repair of Certain Types of Incisional Herniae and Other Conditions, Ann. Surg. **115**:775-781 (May) 1942.

2. Loewe, O.: Ueber Hautimplantation an Stelle der freien Faszienplastik, München. med. Wchnschr. **60**:1320-1321, 1913.

3. Loewe, O.: Ueber Haut-Tiefenplastik, München. med Wchnschr. **76**:2125-2128 (Dec. 20) 1929.

Following the work of Loewe, Rehn [4] (1914) first reported his experimental use of cutis material. His experiments consisted mainly in twisting strips of cutis material and using it as an insert graft after performing a tenotomy on the achilles tendon of dogs. Rehn varied Loewe's technic in removing the epidermis with a razor, thus effecting less trauma to the tissue to be used. He observed that under the influence of continual tension, a gradual degeneration of epithelial characteristics occurred, and the tissue assumed the appearance and function of normal tendon in about ten weeks.

Uihlein,[5] in 1939, reviewed the work of Rehn, and presented a series of 104 cases done in the University Clinic at Freiburg since 1928. He stated that Rehn concluded that cutis is the most suitable material for repairing defects because it most adequately fills the requirements for tissue regeneration.

Cannaday [1] (1942), the first American writer to report the use of cutis grafts in hernial repair in this country, reviewed the literature and presented 14 cases in which he had used cutis material in place of fascial transplants or free fascial grafts in the repair of hernia. In 1943, Cannaday [6] made a later report, adding to his original cases and bringing his total to 37 in which cutis grafts had been used, 27 of which were hernial repairs.

Before going any further, it would no doubt be advisable to qualify and define the term cutis graft. Uihlein [5] stated: "This word was coined by those who suggested the use of this type of skin graft because, though it is derived from the skin, it is not a bona fide skin graft. It does not contain the cutaneous and subcutaneous structures of skin, but it is devoid of its epidermal covering when it is transplanted."

The use of the cutis graft has no doubt been limited because of the mistaken conception that it might lead to the formation of epidermoid cysts. Rehn [7] and his co-workers (1924) demonstrated conclusively from animal experimentation that the cutis graft takes on the characteristics and function of the tissue surrounding it and that in its use in repair of hernia, it forms a strong, fibrous tissue. Loewe [2] had the opportunity to make a microscopic study of pieces of cutis grafts implanted during a previous operation, and observed that the tissue showed retrogression of sweat and sebaceous glands, without cyst formation. Uihlein [5] was able to make a microscopic study of tissue removed from a healed cutis transplant area of 2 patients on whom cutis operations had been done four years previously. He found that the preparations presented normal connective tissue with its fibrous and fatty components containing their own blood and nerve supply, and that the tissues demonstrated an abundant vascularity. He was able to find no epidermal remnant of the original cutis graft and no dermoid cysts could be identified. Peer and Paddock [8] (1937) stored pieces of dermis beneath the skin in a series of plastic reconstruction operations and recovered them later, after varying lengths of time. Microscopic sections of the tissue demonstrated a gradual process of degeneration of normal skin structures, the sweat glands and the hair follicles being the first to disappear, so that

4. Rehn, E.: Das kutane und subkutane Bindegewebe als plastisches Material, München. med. Wchnschr. **61**:118-121, 1914.

5. Uihlein, A., Jr.: Use of the Cutis Graft in Plastic Operations, Arch. Surg. **38**:118-130 (Jan.) 1939.

6. Cannaday, J. E.: Some of the Uses of Cutis Graft in Surgery, Am. J. Surg. **59**:409-419 (Feb.) 1943.

7. Rehn, E., in Lexer, E.: Die freien Transplantationen, Stuttgart, Ferdinand Enke, 1924, pt. 2, p. 503; cited by Uihlein.[5]

8. Peer, L. A., and Paddock, R.: Histologic Studies on the Fate of Deeply Implanted Dermal Grafts, Arch. Surg. **34**:268-290 (Feb.) 1937.

finally a strong, fibrous tissue remained. Our own experimental work with dogs has borne out the results of Rehn [4] and Peer and Paddock,[8] showing the gradual transformation to fibrous tissue and demonstrating that cutis takes on the functions and characteristics of the tissue which it replaces.

In reviewing the literature on the subject, one of us (S. A. S.) was impressed with the difficulty of repair and suturing of the area from which the cutis graft was

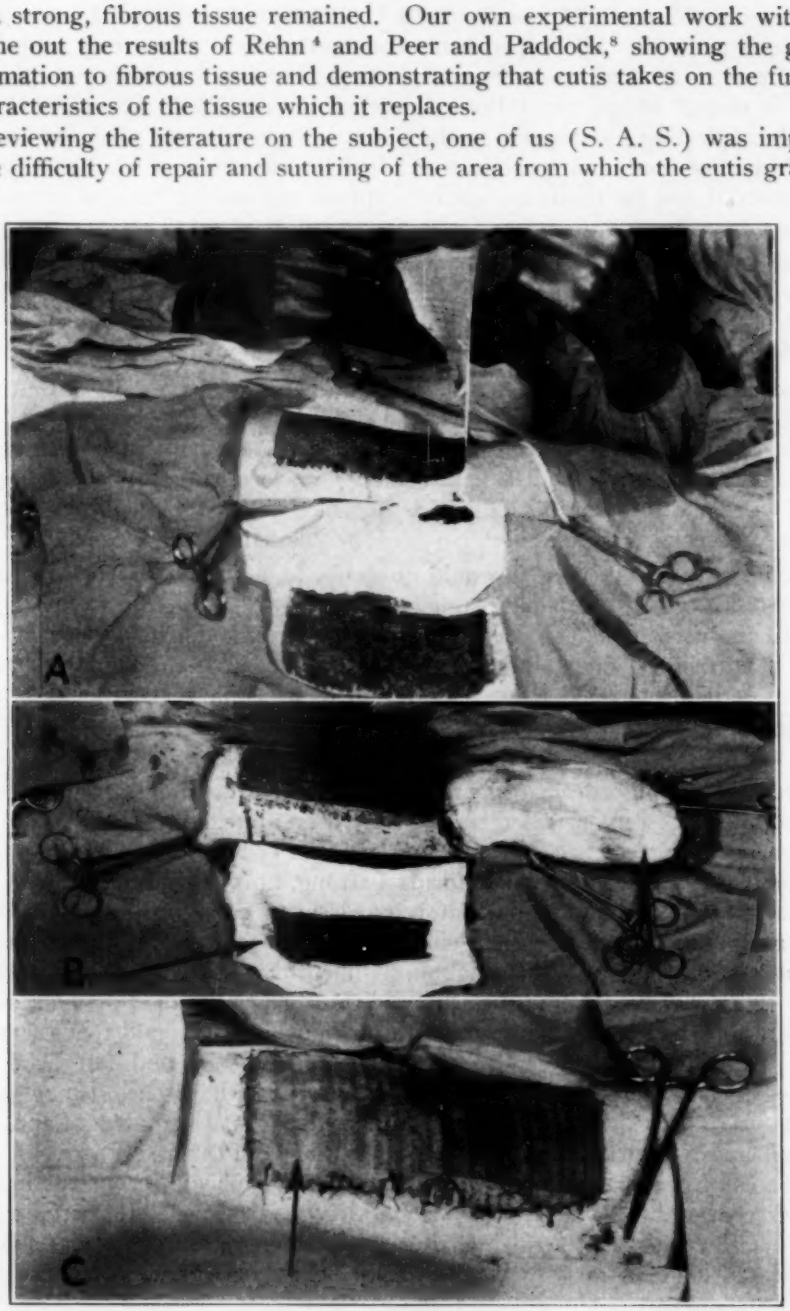

Fig. 1.—*A*, dermatome graft still attached at lower end after removal from right thigh. The blotted pattern of the donor area is shown at the bottom of the figure below the wound. *B*, removal of cutis. The dermatome flap has been reflected down on the moist gauze to the right and is held at the edges with hemostats. The cutis (indicated by arrow) has been removed from the bed of the graft and it is seen that the removed cutis is not quite as large as the graft bed. The removed and slightly shrunken cutis is resting on a piece of gauze below the wound. *C*, restored dermatome flap. The flap has now been sutured back in place with fine silk on all but its attached edge. The arrow denotes the edge of the removed cutis showing through the translucent skin graft.

excised. In his review of Rehn's work, Uihlein [5] gave no indication as to the method of care of the cutaneous wound of the excision area. Cannaday [9] also omitted a description of the repair of the cutaneous defect. As we had had recent experience with the dermatome-flap method of closing a relaxing incision, this technic seemed directly applicable in the closure of the defect in the skin left by the excision of the cutis graft. Thinking that the idea was original, we applied this method to the case which is presented in this paper, only to find that it is almost identically described in Maingot's [10] Post-Graduate Surgery as being done by Rehn in Freiburg. Maingot's description is as follows:

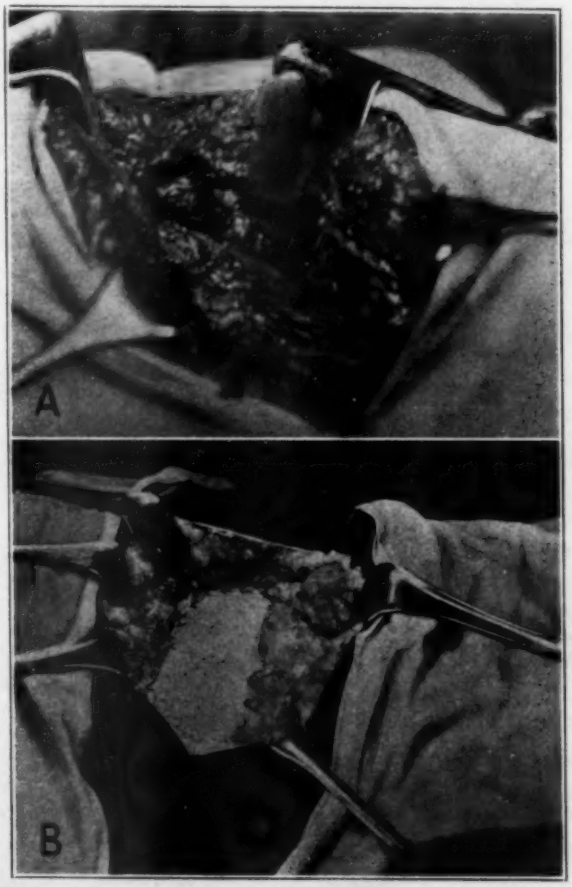

Fig. 2.—*A*, hernial repair by Mayo technic. The cutis has not yet been applied. *B*, application of cutis. The piece of cutis has now been applied over the fascial repair and has been sutured with interrupted silk under moderate tension, both across the bed of the graft and around its edges.

A dermal transplant should be cut to the size of the defect to be covered. After the defect has been defined, a template may be cut in sterile jaconet. With a skin graft razor, of which Humby's pattern is the most reliable when large areas are concerned, a Thiersch graft, some-

9. Cannaday.[1,6] Peer, L. A.: Types of Buried Grafts Used to Repair Deep Depressions in the Skull, J. A. M. A. **115**:357-360 (Aug. 3) 1940.

10. Maingot, R.: Post-Graduate Surgery, New York, D. Appleton-Century Company, Inc., 1937, pp. 3608-3610.

what longer than the dermal patch required, is cut from the outer side of the thigh, but hinged at one end. The jaconet template is applied to the denuded derma, and the required patch cut round and dissected off with some underlying fat. The Thiersch flap is laid back on the raw surface which remains, retained in position with three or four marginal stitches, and pressed down with a firm dressing.

Maingot also states:

While fascial suture will solve most of the problems that can possibly confront the surgeon in the way of repair, it must be remembered that fascia lata, or any aponeurosis transmitting

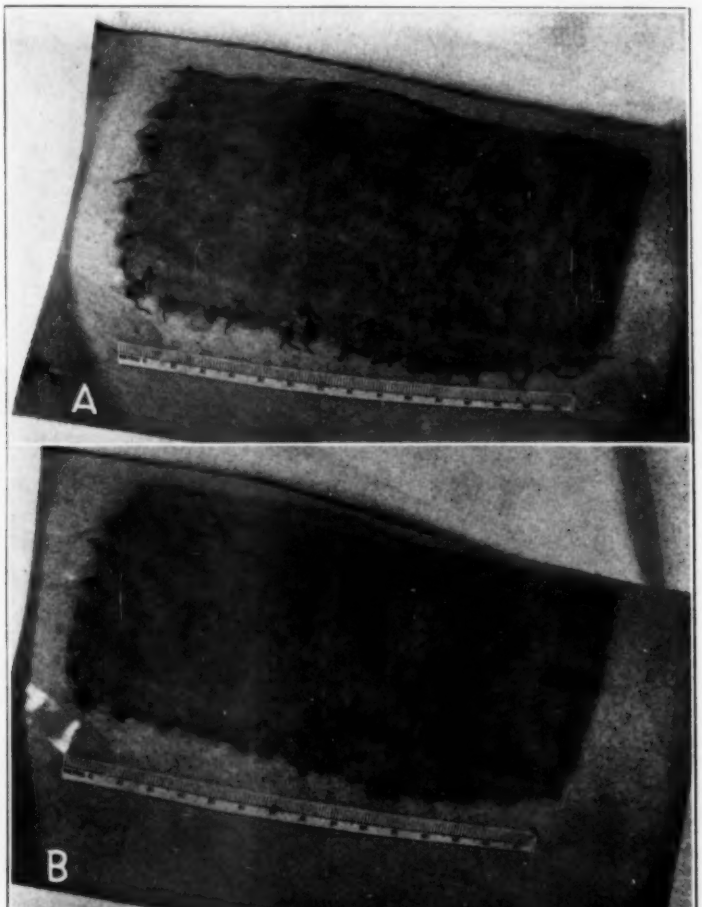

Fig. 3.—*A*, healed donor area on seventh day after operation. *B*, same after removal of sutures. The graft is essentially a 100 per cent take.

the pull of a muscle, is strong only in the direction of that pull. Its longitudinal fibers are held together by very few transverse ones, and large patches, even when securely anchored all round, are quite unfitted to take a strain applied equally to all their margins. The body, however, possesses in the derma a connective tissue sheet of almost unlimited size and strength, a felt-work of tough interlacing fibers equally strong in all directions. We use derma to sole our boots, cover our saddles, drive our machinery; and to paraphrase, one of the oldest sayings runs "there's nothing like derma."

REPORT OF A CASE

L. E., a white man, aged 40 years, was first admitted to the Henry Ford Hospital on April 4, 1940, at which time a diagnosis of nonfunctioning gallbladder was made and operation was advised. Operation on April 9, through a Kocher incision by another surgeon, revealed empyema of the gallbladder. The gallbladder was removed, and the wound was drained. The patient recovered and was discharged on April 26. He returned on Sept. 2, 1942, complaining of a dragging pain in the area of the operative wound, and a diagnosis of ventral incisional hernia was made. Operation was advised, and on September 9 the patient was operated on, at which time multiple peritoneal bulges were evident along the line of the entire incision. A Mayo repair was attempted, but because of lack of good tissue, only a single layer approximation was accomplished. The patient made an uneventful recovery and was discharged on September 24. He was without symptoms referable to the hernia until Feb. 18, 1943, at which time he stated that he again had pain at the incisional site. Examination revealed a recurrent incisional hernia, and operation was done on May 13.

Operation.—In view of the possible depth of penetration of contaminating organisms in the glandular structures of the skin, it is necessary to cleanse the area from which the graft is to be taken with meticulous care. The anterior or lateral surface of the thigh is an ideal

Fig. 4.—Abdominal wound five weeks after operation.

donor site in conditions such as hernias of the abdominal wall. Before the operation, the right thigh was shaved and scrubbed with tincture of green soap for ten minutes. The thigh was then washed with alcohol and ether, and a dry sterile dressing was applied before the patient was taken to the operating room. The entire procedure was done under nitrous oxide anesthesia in order that photographs might be taken.

The dressings were removed from the right thigh, and the area was again washed with alcohol and ether. The size of the desired cutis graft was determined and was marked out on the drum of the Padgett-Hood dermatome by first applying the glue to the entire surface of the drum and then carefully wiping away the glue from the edges with a dry sponge, leaving the glue present over the desired area. The blade of the dermatome was set at five and one-half notches or 0.11 mm. and the split thickness epidermal portion was removed, leaving the lower end to form a flap measuring 25.2 sq. in. (162.59 sq. cm.), as determined with a planimeter (Keuffel and Esser) from a gauze pattern taken at the time of operation and traced on paper, as illustrated in figure 1 *A* and as described by Harkins [11] (1943). The cutis graft was then marked out on the remaining dermis with the scalpel and the tissue, measuring 22.1 sq. in. (142.58 sq. cm.) as determined with the planimeter as just described, was removed by sharp dissection, to but not including the subcutaneous fat, much in the manner of removing a full thickness skin graft, as illustrated in figure 1 *B*. This

11. Harkins, H. N.: A New Type of Relaxing Incision: The Dermatome-Flap Method, Am. J. Surg. **59**:79-82 (Jan.) 1943.

maneuver is greatly facilitated if, after the leading edge is dissected free, that edge is clamped to a roll of gauze bandage. Continued dissection of the graft is done easily, the gauze roll being used as a firm drum on which clean dissection is made possible.

After the graft was removed and placed between layers of gauze soaked in saline solution, the split thickness flap was dropped back on the donor area, in the manner described by one of us (H. N. H.[11]), and was sutured into place, fine black silk being used as illustrated in figure 1 *C*. The grafted area was then covered with petrolatum gauze and an elastic pressure dressing was accomplished by the use of an elastic adhesive bandage.

The field was then shifted to the hernial site, where the scar was excised and dissection was carried down to the sac. After incision of the sac, the fascial edges were identified and were approximated as well as possible, double, heavy silk sutures being used, with an attempt at the overlapping technic of Mayo, illustrated in figure 2 *A*. A small amount of sulfanilamide crystals (not more than 1 or 2 Gm.) was sprinkled on both sides of the graft tissue, and the graft was then sutured in place over the defect with interrupted silk sutures under as much tension as possible, it being made sure that the underlying anterior rectus sheath was devoid of fat and that hemostasis was complete, as illustrated in figure 2 *B*. Additional sutures were further placed around the edges, producing even tension throughout the surface of the graft. Sulfanilamide crystals were then lightly sprinkled over the graft to combat any possible organisms which might be present deep in the dermic structures, and the subcutaneous tissues were approximated with fine silk, dead space being obliterated by inclusion of the surface of the graft in each suture. A small cigaret drain was brought out through the lateral pole of the wound, and the skin was closed with interrupted fine silk sutures.

Postoperative Course.—The drain was removed on the second postoperative day. On this day dyspnea and cyanosis suddenly developed, with a rise in temperature. A diagnosis of pulmonary atelectasis, at the base of the left lung, was made. A large amount of mucus was aspirated from the left bronchus, with much relief to the patient. He was placed in an oxygen tent, which was removed on the fifth day, when the temperature receded to normal. The rest of the postoperative course was uneventful. The dressings on the abdomen and the graft area were changed on the seventh day (May 20, 1943), revealing the split thickness flap graft area healing primarily as illustrated in figure 3 *A*. Sutures were removed from the graft area and abdominal wound on the seventh day, and at no time was there any evidence of a fluid collection in the abdominal wound. Although Cannaday[6] stated that he allows his patients to be out of bed the day after operation, we kept our patient in bed until the fifteenth day, and he was discharged from the hospital on May 31. Subsequent follow-up revealed complete healing of the abdominal wound with excellent support, as illustrated in figure 3 *B*, the photograph being taken June 15. The dermatome flap graft over the cutis excision area has remained perfectly healed, as shown in figure 4.

SUMMARY

A review of the literature on cutis grafts reveals that their use in the United States has been almost entirely limited to the field of plastic surgery.

Cutis material is easily obtainable and is universally applicable in the repair of hernial defects.

The dermatome-flap method of closure of the cutis donor area is presented as previous reports have omitted description of any satisfactory method of closure.

We are carrying on further experimental work on cutis grafts at the present time.

PENETRATING WOUNDS OF THE HEART

A ROUTINE OF MANAGEMENT BASED ON A FIVE YEAR PERIOD OF PERSONAL OBSERVATION AND ON FIVE PERSONAL CASES

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Although wounds of the heart have been diagnosed almost since prehistoric times, their surgical treatment is less than fifty years old, the first two operations, both unsuccessful, having been performed in 1895. Some twenty years earlier the great Billroth,[1] himself a pioneer in many fields of surgery, had written of paracentesis of the pericardium that it approached "very closely to that kind of intervention which some surgeons would term a prostitution of the surgical art and others madness," and had further stated that any surgeon who attempted to suture the living human heart would "lose the respect of his colleagues." In 1896 Stephen Paget[2] said flatly that surgery of the heart had "probably reached the limits set by nature to all surgery; no new method and no new discovery can overcome the natural difficulties that attend a wound of the heart." It is ironic that in that same year Rehn[3] performed the first successful suture of a cardiac wound.

I avail myself of this opportunity to stress the pioneer work of Dr. R. Matas in the field of surgical cardiology, because in this, as in so many other fields related to the progress of surgery, especially at the Charity Hospital, he has led the way not only by his example as a teacher but by the originality, value and volume of his publications which are indicated in the bibliography.[3a]

Examination of the records reveals that the first deliberate thoracotomy at Charity Hospital for a stab wound of the heart was performed on April 7, 1897 by Dr. Matas, who stated in reporting the case: "The chest was opened, the heart exposed and held in the hand in order to search for the wound which involved the wall of the Left Ventricle, but did not penetrate and required no suture." This

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From the Independent Surgical Service of Charity Hospital of Louisiana at New Orleans.

1. Billroth, cited by Elkin.[7]

2. Paget, S.: The Surgery of the Chest, London, J. Wright & Co., 1896.

3. Rehn, cited by Schiebel, H. M.: Stab Wound of the Pulmonary Artery with Suture and Recovery: Report of a Case with a Brief Review of Traumatic Cardiac Surgery, Arch. Surg. **45**:957-963 (Dec.) 1942.

3a. Matas, R.: Surgical Treatment of Perforating and Bleeding Wounds of the Chest, J. A. M. A. **32**:687-692 (April 1) 1899; Surgery of the Chest, Tr. Louisiana State M. Soc., May 1898; Recent Advances in the Technic of Thoracotomy and Pericardiotomy for Wounds of the Heart, Tr. South. Surg. & Gynec. A. **20**:175-188, 1908; South. M. J. **1**:75-81, 1908; Surgery of the Vascular System: Surgery of the Heart and Pericardium, in Keen, W. W.: Surgery: Its Principles and Practice, Philadelphia, W. B. Saunders Company, 1909, vol. 5, chap. 70, pp. 1-350; Military Surgery of the Vascular System: Surgery of the Heart, in Keen, W. W.: Surgery: Its Principles and Practice, Philadelphia, W. B. Saunders Company, 1921, supp. vol. 7, pp. 713-819; Routes of Access to the Heart: Lesions Gathered from the Experiences of the World War, M. Rec. **99**:595-599 and 629, 1921; Personal Experiences in Vascular Surgery, Ann. Surg. **112**:802-839 (Nov.) 1940; Third Presentation on Nov. 14, 1940 of the Matas Award in Vascular Surgery to Dr. Daniel C. Elkin for Outstanding Contributions in Cardiorrhaphy. Proceedings and addresses with special reference to Dr. Matas' discussion of the experiences in suture of cardiac wounds at the Charity Hospital of New Orleans, Report of Committee of Award, New Orleans, Tulane University, 1940, pp. 7-15.

event well antedated the first recorded American cardiorrhaphies, 2 of which were performed by Nietert, of St. Louis, in 1901, the first with operative mortality and the second with complete success.

Until very recent years, however, cardiorrhaphy remained in the nature of a surgical *tour de force,* and reports of its performance were chiefly the records of single cases. The literature on the subject is still confused, and even in the most careful reviews it is difficult to determine how much collected series overlap. Furthermore, it is clear that the rate of success has always seemed larger than it actually is, because statistics seldom take into account the number of patients with wounds of the heart who die without diagnosis, who die without treatment or who die after unreported operations. There is no doubt, for example, that among the 1,612 stab wounds of the chest treated at the Charity Hospital of Louisiana at New Orleans over the ten year period ending Dec. 31, 1940 were some undiagnosed wounds of the heart.

In 1934 Ramsdell [4] collected 428 surgical cases reported prior to Jan. 1, 1932, in which the mortality ranged from 24 to 75 per cent and averaged 50 per cent. In the same year von Remetei [5] mentioned a series of 535 surgical cases with a mortality of 55 per cent. Recently several relatively large single series have been reported, in which the distribution of the incidence and mortality furnishes interesting contrasts. Bigger,[6] who reported 25 operations with 9 deaths in 1940, pointed out that the first cardiorrhaphy in the Medical College of Virginia Hospital was not performed until 1930, but that 25 such operations were performed in the next nine years. Elkin,[7] who reported 38 operations with 16 deaths from Emory University Hospital in 1941, stated that the number of treated wounds of the heart had increased steadily each year since 1930. McGuire and McGrath [8] reported in the same year that the mortality from wounds of the heart at the Cincinnati General Hospital prior to 1937, when conservative therapy or aspiration (if tamponade was present) was the practice, was 82 per cent. After that time, when operation became the rule in all diagnosed cases, the mortality fell to 23 per cent (3 of 13 operations). Griswold and Maguire,[9] writing in 1942, stated that prior to 1933 only 3 operations on the heart, only 1 of which was successful, had been performed at the Louisville City Hospital. Since that date 22 operations had been done, with 6 deaths, and only 1 death had occurred in the last 13 cases.

Analysis of cardiac wounds at the Charity Hospital of Louisiana at New Orleans shows a precisely similar trend. Matas previously tabulated all of the recorded cardiorrhaphies at Charity Hospital from the first (and successful) one, done in January 1913 by Dr. Joseph Danna, to one done in October 1940 by Dr. Mims Gage. There were 17 operations by eight surgeons, with 11 deaths, or a mortality of 65 per cent.

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4. Ramsdell, E. C.: Stab Wounds of the Heart, Ann. Surg. **99:** 141-151 (Jan.) 1934.

5. von Remetei, F. F.: Ueber die Stichverletzungen des Herzens nebst zwei Fällen, Zentralbl. f. Chir. **61:** 1723-1726 (July 21) 1934.

6. Bigger, I. A.: The Diagnosis and Treatment of Heart Wounds, with a Summary of Twenty-Five Cases, South. M. J. **33:** 6-11 (Jan.) 1940.

7. Elkin, D. C.: The Diagnosis and Treatment of Cardiac Trauma, Ann. Surg. **114:** 169-185 (Aug.) 1941.

8. McGuire, J., and McGrath, E. J.: Penetrating and Lacerating Wounds of the Heart, Tr. A. Am. Physicians **56:** 194-200, 1941.

9. Griswold, R. A., and Maguire, C. H.: Penetrating Wounds of the Heart and Pericardium, Surg., Gynec. & Obst. **74:** 406-418 (Feb., no. 2 A) 1942.

I am now able to report a series from February 1940 to October 1943 of 11 cardiorrhaphies by six surgeons, with 1 death, a mortality of 9 per cent. Of this group I personally performed 5 and am responsible for the single death.

The surgeons who have performed the operations reported in the entire series, from 1913 to 1943, are (chronologically) Drs. J. Danna, G. Graffagnino, E. Irwin, M. O. Miller, J. Landry, F. Planche, M. Gage, A. Ochsner, H. Kahle, R. Hays, H. Nelson, D. Williams, J. DiLeo and G. Martin.

The striking increase in the number of cardiorrhaphies performed at Charity Hospital in recent years is not due to any increase in the incidence of cardiac wounds but rather to a change in the surgical point of view concerning them. More correct diagnoses are being made because wounds of the heart are being suspected in more cases of thoracic injury. More operations are being performed on patients suspected of having wounds of the heart because the resident staff, which for obvious reasons handles the majority of such cases, is better informed concerning them, because of the rapidly accumulating store of information in the periodical literature, if for no other reason.

This information, incidentally, is chiefly contained in the periodical literature. Textbook discussions of the subject are for the most part thoroughly unsatisfactory. They usually consist of a discussion of cardiac tamponade, with therapeutic advice confined to the statement that only prompt operation can save the patient. It is to be hoped that new texts and new editions of standard texts will include the valuable material now available in the recent surgical journals.

DIAGNOSTIC CONSIDERATIONS

The diagnosis of cardiac wounds has been so excellently discussed by so many writers that not a great deal need be said about it here. It is not particularly difficult when the classic picture is present, including: (1) a period of freedom from symptoms, followed by rapid collapse and unconsciousness; (2) weak heart sounds associated with a weak pulse; (3) lowered arterial pressure, and (4) elevated venous pressure. Not a great deal of emphasis, however, has been placed on the fact that this picture is not present in all cases, particularly in cases in which automatic decompression occurs and tamponade is absent because the wound in the pericardium communicates with the pleural cavity or with the external surface of the body. Blegen [10] is one of the few writers to call attention to this phenomenon.

Many lives will be lost unless there is constant emphasis on the fact that a wound of the heart is a possibility in any instance of penetrating thoracic injury, particularly when there is evidence of (1) cardiac tamponade, (2) progressive tension pneumothorax, (3) marked or progressive hemothorax and (4) shock other than that resulting purely from traumatic stimuli. These criteria, alone or in combination, furnish absolute indications for exploration of the chest. This opinion is based on a five year period of clinical observation in the Charity Hospital of Louisiana at New Orleans, which, with its large Negro population, offers a wide experience with wounds of violence.

A consideration of the phenomena of shock and of their background furnishes further support for prompt exploration in all cases in which diagnosis is not immediately evident. Watchful waiting, as Moon [11] has cautioned, is likely to be

10. Blegen, H. M.: Wounds of the Heart: A Review of Seventeen Cases with Four Operations, Journal-Lancet **63**: 1-7 (Jan.) 1943.

11. Moon, V. H.: Shock: Its Dynamics, Occurrence and Management, ed. 2, Philadelphia, Lea & Febiger, 1942.

disastrous with any condition in which shock may develop. A patient in shock presents a vicious cycle initiated by hemorrhage, going on to hypotension and culminating in anoxia or hypoxia, which would seem the preferred term as more accurately expressing a decrease below physiologic limits in the supply of oxygen available for the tissues. Hypoxia is also aggravated by decreased vital capacity incidental to fluid in the pleural cavity or to tension pneumothorax. Both experimental and clinical observations show that not a great deal of hemorrhage is necessary to set in motion this vicious cycle and that the loss of small quantities of blood, which would be insignificant in a normal subject, may be lethal to a patient suffering from shock from any cause.

It is also important to emphasize again the now well known fact that a patient suffering from incipient shock or already in a state of shock may present no immediate clinical evidence of his condition. Blalock,[12] Moon [11] and others have repeatedly pointed out that the vital signs are an unreliable guide to the state of the circulation in incipient shock and that a progressive decline in the arterial pressure, with its accompanying evidences of circulatory deficiency, should be interpreted not as evidence of impending shock but rather as evidence of departed opportunities for treatment.

My associates and I have repeatedly corroborated these observations at the Charity Hospital of Louisiana at New Orleans. Patients with thoracic wounds, in whom the extent of the injury was not immediately apparent, have been kept under constant careful observation and yet either have died while under observation or have deteriorated so rapidly as to preclude surgical intervention. It has also been observed that patients who were brought out of primary shock but who again entered a state of shock while conservative therapy was practiced were unlikely to recover, regardless of the adequacy of later treatment. This clinical observation substantiates Blalock's [12] experimental demonstration that prolonged hypotension due to repeated bleedings is attended with a mortality of 100 per cent, even though the quantity of blood provided by transfusion actually exceeds the amount of blood withdrawn.

The final argument for exploratory thoracotomy in cases of suspected cardiac damage is that the exploration is attended with a minimal mortality. During five years of observation in the accident and emergency surgical service at Charity Hospital, I have never seen a death attributable to simple opening of the chest for exploratory purposes.

THE ILLOGIC OF CONSERVATIVE THERAPY FOR CARDIAC TRAUMA

The most valid reason for resorting to prompt operation for cardiac wounds is that a long trial of conservative therapy over many years has shown that in spite of occasional brilliant results the mortality of this method is very high. It was 90 per cent in the 452 cases of penetrating wounds of the heart collected by Fischer [13] in 1868. That some patients recover without operation is no argument for nonsurgical therapy, in view of the impossibility of determining in which cases that happy outcome will be achieved.

Incidentally, the fact that a patient is apparently moribund should not deter one from operating. Bullock's [14] suggestion is sound, that even a moribund sub-

12. Blalock, A.: Shock: Further Studies with Particular Reference to the Effects of Hemorrhage, Arch. Surg. **29**: 847-857 (Nov.) 1934.

13. Fischer, G., cited by Blegen.[10]

14. Bullock, W. O.: The Ultimate Phase of Life as It Relates to Wounds of the Heart, Ann. Surg. **103**: 696-697 (May) 1936.

ject should be submitted to what Blegen [10] has called "a quick thoracic autopsy," which would be his only hope of salvation. In Bullock's own case the patient was thought to be dead before the pericardium was opened, but operation was proceeded with (in order, Bullock stated frankly, that he might gain experience in operating on the heart) and survival followed.

Another argument against conservative therapy is that it may be followed by undesirable consequences. Rehn,[3] who performed the first successful cardiorrhaphy on record, advocated suture of the wound if only because an unsutured wound might leave a weak heart. Elkin [7] and Strieder,[15] writing along the same lines, have both pointed out the possibility of the development of aneurysm of the coronary vessels or of the myocardium. Another objection to conservative therapy is the possible development of pericardial adhesions. A case of this sort was observed at Charity Hospital. The patient presented symptoms of heart failure, which had first appeared after conservative treatment of a wound of the heart at another institution. A diagnosis of pericardial adhesions was made and cardiolysis was attempted, but the adhesions were too dense and widespread to be released and death followed.

Aspiration of the pericardial cavity, whether as a method of diagnosis or of treatment, is mentioned only to be condemned. It furnishes no information not usually available by other methods, its permanent therapeutic value is always debatable, and it may do considerable harm. In 1 case in which it was practiced at Charity Hospital the patient died instantly. Autopsy showed that the needle had penetrated one of the coronary vessels.

ROUTINE OF MANAGEMENT

The management of suspected or proved wounds of the heart at Charity Hospital is based on the concept that cardiac hemorrhage does not differ from any other variety of internal hemorrhage and that the best opportunity for survival in any case of internal bleeding is offered by prompt control of the bleeding, perferably at the source.

A patient with a penetrating thoracic wound in which absolute indications for exploration of the chest are not present is submitted to a period of observation and diagnostic testing, which never exceeds thirty minutes. During this period all preparations for operation are carried out. He is placed in the Trendelenburg position, and morphine and scopolamine are given in doses appropriate to his weight and age. Oxygen inhalations (by mask or tent) are also begun at once. If prompt and progressive improvement ensues under these measures, it is assumed that the state of shock has resulted from traumatic stimuli rather than from persistent hemorrhage or pulmonary compression or a combination of these conditions. A patient who does not improve promptly is given the benefit of an exploratory thoracotomy.

The wound is examined under aseptic precautions as soon as sedatives have been administered. A wound made with a knife or other large instrument is usually immediately perceptible, but careful examination may be necessary to identify a wound made with an ice pick or a similar small weapon. A sucking wound is closed with a pressure dressing, and treatment for tension pneumothorax is begun. Mediastinal emphysema is treated by incision above the manubrium sterni and insertion of a rubber catheter into the mediastinum. Unless these two

15. Strieder, J. W.: Stab Wound of the Heart: Report of a Case Treated Conservatively, J. Thoracic Surg. **8**: 576-577 (June) 1939.

complications demand immediate treatment, a simple sterile pressure dressing is placed over the wound while further diagnostic measures are proceeded with.

The point of maximum impulse is indicated on the wall of the chest and is observed frequently, to detect a possible shift of the mediastinum. The pulse, respiratory rate and blood pressure are checked at frequent intervals, as is the venous pressure. The venous pressure is usually elevated in patients with cardiac wounds, but a low pressure is not incompatible with this type of injury and would be expected in shocked patients or in patients in whom automatic decompression of the pericardium is possible. Diagnosis in this type of case may be extremely difficult, but in cases in which the venous pressure is greatly elevated a high degree of tamponade may be assumed and operation should be proceeded with at once.

Repeated determinations of the blood concentration are useful in detecting incipient shock. Roentgen examination is sometimes helpful in demonstrating the extent of the initial hemothorax and pneumothorax but is unreliable in demonstrating the existence of hemopericardium.[7] Bigger[6] has emphasized the value of fluoroscopy in demonstrating the obliteration of pericardial pulsations and the immobilization of the heart shadow, but our policy of performing an exploratory operation in all doubtful cases makes this diagnostic aid unnecessary. Electrocardiographic study is not employed as a preoperative measure.

Typing and cross matching of blood are carried out in all cases, and transfusion, preferably with whole blood, is begun as soon as a supply of blood or plasma is available in all cases in which exploration is to be done. The replacement of blood is so important that autotransfusion was employed in 1 of my early personal cases. The establishment of a blood and plasma bank at Charity Hospital made this measure unnecessary in later cases. The blood is introduced through an intravenous cannula, since experience has shown that its free and uninterrupted flow may mean the difference between life and death. The rate of flow, however, is always slow until the cardiac wound has been closed.

External heat is the only routine antishock measure which is not employed. It has been found that reduction of the environmental temperature by thermostatic control (the emergency and operating rooms at Charity Hospital being air-conditioned) gives better results than the use of heat.[16] Unless the stomach is known to be empty it is emptied by suction before anesthesia is begun.

ANESTHESIA

My preference is for cyclopropane or ethylene-ether anesthesia, which should be given by a skilled anesthetist and by the endotracheal route.[16a] This form of anesthesia maintains a constant and adequate airway, provides adequate relaxation and yet at the same time furnishes a maximum concentration of oxygen, a consideration of paramount importance for a patient suffering from actual or potential hypoxia. McGuire and McGrath[8] attributed a high percentage of pulmonary complications

16. Cooling in Shock, editorial, J. A. M. A. **121**: 432-433 (Feb. 6) 1943.

16a. This method of anesthesia was initiated by Dr. Matas with his modification of the Fell-O'Dwyer tube which he introduced at Charity Hospital in 1899. His apparatus allowed the introduction of chloroform or ether vapor with positive pressure. (Matas, R.: On the Management of Acute Traumatic Pneumothorax, Ann. Surg. **29**:409-434, 1899; Intralaryngeal Insufflation for the Relief of Acute Surgical Pneumothorax: Its History and Methods with a Description of the Latest Devices for This Purpose, Tr. South. Surg. & Gynec. A. **12**:52-84, 1900; Artificial Respiration by Direct Intralaryngeal Intubation with Modified O'Dwyer Tube and New Graduated Air-Pump [Matas-Smyth Pump] in Its Application to Medical and Surgical Practice, Tr. Am. S. A. **19**:392-411, 1901; Am. Med. **3**:97-103, 1902.)

in their series of cases to the use of general anesthesia, but this has not been my experience. Local infiltration has been advised by several writers, but I am opposed to it for at least three reasons: 1. It is time consuming. 2. It does not permit the endotracheal airway possible in inhalation anesthesia. 3. It furnishes no control over the patient's movements. Patients with cardiac wounds are frequently under the influence of alcohol, and their clouded mental state is often aggravated by the cerebral manifestations of hypoxia.[17] As a result, their uncontrolled movements under local analgesia may do a great deal of harm.

SURGICAL TECHNIC

The chest is opened by a transverse incision with a vertical extension along the parasternal line, the location of the incision depending on the location of the injury. A single rib is resected subperiosteally, and such additional space as is necessary is provided by the simple division of one or more adjacent ribs. The extrapleural approach is undesirable for several reasons. It is more time consuming than the transpleural approach. Exposure is less satisfactory. Pleuropericardial drainage is not obtained. No matter how careful the technic, the pleural cavity is often opened accidentally. Bigger [6] has called attention to this accident, and it has been observed in several cases at Charity Hospital. Finally, and most important, the extrapleural approach serves no useful purpose, since the pleural space must always be explored for possible damage to the lung and to adjacent vessels.

If possible, the traumatic wound is excised when the surgical wound is made. If this is not possible, it is carefully isolated until the close of the operative procedure. Then it is debrided, irrigated and insufflated with sulfathiazole powder before it is sutured. Infection of the wound is a serious possibility in cardiac trauma. I have followed this plan in all 5 of my cases and have never witnessed it personally.

If careful exploration of the pericardium reveals no evidence of laceration or of contained blood, it is not opened and the possible damage caused by the penetrating wound is sought for elsewhere. Otherwise the pericardium is incised vertically along its lateral surface. All preparations have previously been made to place at least one suture instantly if the cardiac wound presents at the opening, before forcible cardiac contraction returns with the relief of tamponade. Occasionally it is possible to place all the sutures before forcible contraction returns. Aspiration of the contained pericardial blood and clots is then carried out. This technic greatly simplifies the insertion of sutures in the heart and is usually possible if the surgeon is alert to grasp the opportunity.

If the wound does not immediately present, 1 per cent solution of procaine hydrochloride is injected into the vagus nerve before any further manipulation is attempted. The rationale of this step is the observation by anesthetists that traction on the heart or bronchus is likely to be followed by bradycardia or cardiac asystole, the risks of which need no elaboration. The plan was suggested to me by the studies of Weiss and Ferris [18] on the hyperactive carotid sinus reflex, and I feel that occasional deaths from cardiac asystole will be prevented by its use.

The use of a traction suture, in my opinion, is always undesirable. The heart can be rotated manually quite as satisfactorily and with less trauma. Furthermore,

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17. Batten, C. T., and Courville, C. B.: Mental Disturbances Following Nitrous Oxide Anesthesia, Anesthesiology **1**: 261-273 (Nov.) 1940.

18. Weiss, S., and Ferris, E. B., Jr.: Adams-Stokes Syndrome with Transient Complete Heart Block of Vagovagal Reflex Origin: Mechanism and Treatment, Arch. Int. Med. **54**: 931-951 (Dec.) 1934.

a traction suture occasionally tears through, as happened in 1 case observed at Charity Hospital.

The heart wound is closed with interrupted cotton intestinal sutures. Sutures of this material, as Meade and Ochsner [19] have shown, produce a minimum of reaction in the tissues. If hemorrhage complicates the closure or makes it impossible, gentle digital pressure directly over the defect is usually effective. The finger, as Beck [20] warns, should not be placed in the wound, from which it would be forced out with each beat of the heart, but over it. If this plan is not effective the Sauerbruch [21] maneuver should be employed: The vena cava is compressed by passing the left hand between it and the transverse sinus. Compression should be very brief. The coronary vessels should be visualized, so that sutures will not be placed through them or include them.

After the presenting wound has been closed, the entire heart is inspected for possible further damage. In 4 of the cases observed at Charity Hospital the wounds were multiple, and in 1 instance the second wound was not found until the patient had died on the table after closure of what was thought to be a single wound.

The pericardium is now cleared of accumulated blood and clots, irrigated with warm isotonic solution of sodium chloride and closed with a row of interrupted cotton sutures. A small opening is left at the upper angle for drainage. I prefer drainage in this area to the more commonly employed drainage opening at the inferior angle of the wound. The lower opening drains off not only excess pericardial fluid but also normal amounts, which should be left in situ to prevent friction and subsequent inflammation. No other form of drainage is employed unless suppuration is definitely anticipated.

After the pericardium has been closed, the lung, mediastinum, diaphragm and mammary and intercostal vessels are inspected for possible damage, which is corrected according to the indications. The pleural cavity is then irrigated with warm isotonic solution of sodium chloride, both to check for a possible leak of air and to reduce by dilution possible bacterial contamination. After the solution has been suctioned out, sulfathiazole (5 Gm.) in suspension is placed in the cavity and the wound is closed about an oxygen catheter with interrupted cotton sutures. Separate closure of the pleural layer is not necessary. The catheter is removed just before the last suture is tied, and the excess of oxygen is removed by suction. The replacement of the intrapleural atmosphere by oxygen was first practiced in Overholt's [22] clinic by Betts and Cotton, to whom it was suggested by Welkin and Herman's work on rapid reexpansion of the lung after the institution of pneumothorax in tuberculosis. Pulmonary reexpansion should never be accomplished by manual compression of the anesthetic bag, because of risk of trauma to the alveoli.

POSTOPERATIVE THERAPY

Some patients who would otherwise have survived operation on the heart have probably lost their lives because of poorly directed or actually inadequate postoperative therapy, and too much importance cannot be attached to this phase of treatment. It has several objects: (1) the prevention or correction of hypotension,

19. Meade, W. H., and Ochsner, A.: Spool Cotton as a Suture Material, J. A. M. A. **113**:2230-2231 (Dec. 16) 1939.

20. Beck, C. S.: Further Observations on Stab Wounds of the Heart, Ann. Surg. **115**: 698-704 (April) 1942.

21. Sauerbruch, cited by Elkin.[7]

22. Overholt, R. H.: Personal communication to the author.

(2) the prevention or correction of hypoxia, (3) the prevention of cardiac tamponade, (4) the prevention of cardiac failure and (5) the achievement of maximum repair of the tissues.

The closure of the cardiac wound, the transfusion of an adequate amount of blood and the administration of oxygen are usually followed by correction of hypotension. The patient is kept on the operating table until this object is achieved. Transfer to the ward before the arterial pressure has been stabilized at an approximately normal level is unwise, since the pressure may drop still further in transit. If the pressure does not rise within a reasonable time, a fatal outcome is likely, since hypoxia and irreversible injury to the central nervous system are consequences of prolonged hypotension.

On his arrival in the ward, the patient is placed in a tilted bed, with the head elevated. This position makes respiration easier and is a prophylaxis against peripheral vascular thrombosis. Morphine is used in amounts barely sufficient to control pain, because of its tendency to depress the respiratory centers and thus aggravate hypoxia. Oxygen is given continuously by mask or tent. Additional transfusions are given if the hemoglobin or red blood cell count is low, and plasma is used if the concentration of the blood is abnormally high or if the serum protein content is low. Otherwise a proper fluid balance is maintained by carefully regulated intravenous infusions of dextrose and isotonic solution of sodium chloride. Chemotherapy is employed only on definite indications. Vitamin concentrates, especially ascorbic acid, are administered in large doses. Bigger,[6] who lost a patient in whom a clot completely filled the right ventricular cavity, has proposed the use of heparin after operation if the wound has penetrated any of the chambers of the heart or has divided important coronary vessels, and the rationale of the suggestion is clear. Practical considerations, however, make the general employment of this method unlikely.

The patient is not permitted out of bed for at least three to four weeks, and it is impressed on him that his resumption of his usual activities must be carefully graded.

The most important postoperative complications are: atelectasis, pulmonary compression and pneumonitis, all of which are related to hypoxia; pericarditis, which causes tamponade, and myocardial infarction.

Prophylaxis against atelectasis includes moving the patient from his back to the involved side at intervals, until he is able to move himself, and encouragement of coughing and deep breathing exercises. The onset is heralded by hyperpyrexia and by the usual symptoms of hypoxia, namely, hyperpnea, elevation of the pulse rate, elevation of the arterial pressure and sometimes psychotic manifestations. It should be emphasized that diffuse bilateral atelectasis may occur with few or no demonstrable physical findings. The statement that the absence of cyanosis implies adequate oxygenation is by no means true. Lundsgaard and Van Slyke [23] demonstrated many years ago that for physical reasons cyanosis cannot appear in patients who have less than 5 Gm. of hemoglobin per hundred cubic centimeters of blood, because of the dilution of their blood. In other words, the paradoxic situation exists that the patient most likely to have fatal hypoxia, because of his lack of hemoglobin, is least likely to manifest cyanosis, while the patient whose condition is much less critical is more likely to present it, because his supply of hemoglobin is adequate.

23. Lundsgaard, C., and Van Slyke, D. D.: Cyanosis, Medicine **2**: 1-76 (Feb.) 1923.

If atelectasis should occur, postural drainage and aspiration with a bronchial catheter should be carried out without delay. If this aspiration is unsuccessful, bronchoscopic aspiration should be carried out with equal promptness.

Pulmonary compression which develops soon after operation is usually the result of either tension pneumothorax or hemothorax. Tension pneumothorax is treated by the immediate insertion of an intrapleural cannula connected with a water trap. Minor degrees of hemothorax need only careful observation. Progressive hemothorax is treated by aspiration, supplemented by transfusion as necessary. Neither tension pneumothorax nor hemothorax is likely to occur if exploration and operative technic have been adequate.

Delayed pulmonary compression is usually the result of pleural effusion, the development of which can be foreseen in routine serial roentgenograms. The fluid is removed only if it is present in sufficient amounts to cause symptoms or if there is undue delay in pulmonary reexpansion. An occasional and seldom remembered cause of pulmonary compression is elevation of the diaphragm as the result of gaseous distention of the intestinal tract. In such circumstances dyspnea may be alarming, and relief is dramatic when gastroduodenal suction, the rectal tube and enemas are used.

The management of pneumonitis and of myocardial infarction does not differ from their management under other circumstances. The taking of serial electrocardiograms is a wise precaution after operation, particularly if the coronary vessels have been implicated in the wound. In 1 such case at Charity Hospital serial electrocardiograms showed typical coronary occlusion. Improvement was progressive, but a symptomless myocardial infarct was still present when the patient disappeared from observation about four months after operation.

ANALYSIS OF CASES

From Jan. 1, 1906 to the date of writing 27 cardiorrhaphies have been performed by 13 surgeons at the Charity Hospital of Louisiana at New Orleans. I performed 5 operations, with 1 death, and Dr. Mims Gage [24] performed 4, with 1 death. The death of my patient was entirely preventable and should not have occurred: The patient presented a good risk, and operation was undertaken promptly and carried out without special difficulty. Because of a confusion of priorities, however, the hospital supply of oxygen masks and tents had been exhausted, and oxygen in high concentration could not be supplied. Autopsy revealed left ventricular dilatation, a small pleural effusion and moderate bilateral pulmonary edema. None of these was sufficient in itself or in combination with other pathologic changes to explain the death; all of them, however, pointed to hypoxia as the basic cause of the fatality.

All 27 patients were Negroes, and all but 1 were men. The majority were under 30 years of age, but 2, 50 and 53 years of age respectively, are among the oldest recorded in the literature. Dr. D. B. Williams,[25] who has already reported the case, operated on the 50 year old subject, and I operated on the 53 year old man. Curiously, the ice pick, on which Elkin, whose experience is chiefly with Negroes, has frequently laid stress, was used in only 1 instance in the Charity Hospital series. All the other injuries were caused by knives of various sizes. All

24. While the proof was being corrected, Lieutenant Colonel Mims Gage accomplished another successful cardiorrhaphy while functioning as a medical officer in the Fourth Service Command.

25. Williams, D. B.: Successful Suture of Stab Wound of Heart, New Orleans M. & S. J. **95:** 470-472 (April) 1943.

the implements had been removed, either by the assailants or by the victims themselves, before hospitalization, and the diagnostic aid furnished by the coincident movement of the weapon and the heart was thus not present in any of these cases.

In the reports on 2 patients operated on early in this series no statement is made as to the location of the wound. In the remaining 24 cases the wound involved the apex in 1, the anterior surface in 1, the left atrium in 3, the right atrium in 5, the left ventricle in 9 and the right ventricle in 10. Elkin [7] also found the highest incidence (14 of 38 cases) in the right ventricle and attributed it to the fact that this ventricle occupies the greater part of the anterior portion of the heart.

In 4 cases the wounds were multiple. In the first case there were two wounds of the left ventricle. In the second case the wound involved the right ventricle and the right atrium. In the third case it involved the right atrium and both ventricles. In the fourth case it involved the right ventricle and the right atrium. The last 2 patients, who were operated on by Dr. Mims Gage and Dr. J. L. DiLeo respectively, both survived. The longest wound, which I personally sutured, measured approximately 2.75 cm. and required six stitches.

The postoperative complications in the last 11 cases in this series included pleural effusion in 8 cases, in 1 of which it was bilateral, wound infection in 2 cases, and myocardial infarct and hemothorax in 1 case each. Tension pneumothorax, postoperative hemorrhage, postoperative tamponade, empyema and pulmonary complications were conspicuously lacking.

Associated pathologic states included laceration of the internal mammary vessels in 2 cases and of the coronary vessels in 1, a sucking thoracic wound in 1, and periapical pulmonary adhesions in 2. A sucking thoracic wound, if not promptly closed, is likely to bring on hypoxia rapidly, since it causes bilateral pulmonary compression. Periapical adhesions, which must be divided before the lung can be brought down and the pericardium exposed, prolong the operative procedure and increase the technical difficulties.

One patient I operated on had a preexistent pneumonitis. He had had bilateral bronchopneumonia and was left unattended while members of his family were working in the barroom over which they lived. While they were absent he slipped out of bed, left the house by a back door and went to another barroom, where he was stabbed in the heart. Fortunately, the pulmonary condition was readily controlled by chemotherapy.

The reduction in the mortality of cardiac wounds at Charity Hospital in the last three years can be attributed to a number of causes. One of the most important is the institution of a strict regimen of management, which means that when the patient reaches the hospital no time is lost in placing him on the operating table. The lapsed time between admission and operation in 1 of these cases was only fifteen minutes. The regimen of postoperative therapy is planned as carefully as the preoperative regimen, and a continuing endeavor has been made to develop an atraumatic technic, the steps of which have been described. Skilful anesthesia and the immediate availability of blood and plasma are other important reasons for the lowered mortality. Chemotherapy was used in all but 1 of the last 11 cases, but only on definite indications. The value of the sulfonamide drugs is granted, but it is felt that their role in the lessening of the mortality of cardiac wounds has been small. The basic cause for the reduction of the mortality is, as already indicated, the adoption of an attitude of suspicion, so that exploration is carried out in every instance of penetrating thoracic wound in which it cannot be said positively that a cardiac wound does not exist.

SUMMARY AND CONCLUSIONS

In recent years the number of operations for wounds of the heart has increased and the mortality has decreased. The 11 cardiorrhaphies performed in the last three years at the Charity Hospital of Louisiana at New Orleans, 5 of which I performed, reflect both these trends.

A detailed outline of preoperative management, anesthetic methods, surgical technic and postoperative therapy is presented.

Conservative therapy of cardiac wounds has given poor results, and there is no valid reason why such a wound should not be handled precisely as any other wound in which hemorrhage is a factor, that is, by control of the bleeding at the source.

The recent reduction in the mortality of cardiorrhaphy can be attributed to several causes, including promptness of operation, adherence to a detailed regimen of management throughout the case, and skilled anesthesia. The most important reason for the reduction, however, is the policy of performing an exploratory operation in all cases of penetrating thoracic wounds in which it cannot be determined positively that the wound has not reached the heart.

Dr. John Adriani, director of anesthesia at the Charity Hospital of Louisiana at New Orleans, gave invaluable suggestions regarding anesthesia and postoperative care. Miss Elizabeth McFetridge assisted in the preparation of the paper.

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A FLEXIBLE PLASTIC-LIQUID ADHESIVE

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The irritations, abrasions and dermatitis produced by adhesive plaster when used with wound dressings are too well known to require elaboration. In addition, there are many patients for whom adhesive plaster cannot be used at all, owing to allergies and extreme sensitiveness of the skin to the plaster. Two other disadvantages invariably connected with the use of adhesive plaster in surgical dressings are the varying degrees of discomfort to the patient and the necessity for removing adhesive debris with solvents that may further irritate the skin.

The foregoing objections led to a search for a substance which could be used in place of adhesive plaster and which would have the following characteristics: (1) adhesive qualities, (2) elasticity, (3) ease of application, (4) ease of removal without debris, (5) freedom from toxic and allergic effects, (6) ready availability, (7) low cost and (8) freedom from staining.

In order to achieve these effects, an experiment was conducted at Montefiore Hospital for Chronic Diseases in which adhesive plaster made from natural resins was replaced with a liquid adhesive made from synthetic resins.

Solutions of polyvinyl butyral resin in varying solvents and containing different plasticizers were applied to dressings and the skin in order to arrive at a combination of ingredients which would be most efficient for the purpose intended. The following formula was found to produce a liquid which possesses adequate adhesive qualities and elasticity, is capable of easy removal without leaving debris on the skin and is readily available and inexpensive:

Polyvinyl butyral resin[1]	20 Gm.
Alcohol (95 per cent)	120 cc.
Ether	20 cc.
Castor oil	10 cc.

The polyvinyl butyral resin is placed in the mixture of alcohol and castor oil and allowed to dissolve without stirring or agitation (admixture of air must be prevented). When the polyvinyl butyral resin is completely dissolved, the ether is added. The resulting solution is a clear, colorless liquid of high viscosity.

If the liquid is used, for example, on a gauze dressing 8 inches (20 cm.) square and ½ inch (1.3 cm.) thick, it should be applied along a border 1 inch (2.5 cm.) to 2 inches (5 cm.) wide with a wooden applicator or spatula and the wet surface of the dressing should be placed against the skin. Pressure with the hand should be used for about one minute on the border of the dressing. This will make for quicker and better adhesion.

In order to determine whether the adhesive solution was irritating or capable of producing toxic reactions, or inducing allergies, tests were conducted on 175 patients in the Pulmonary Division of Montefiore Hospital and in the Montefiore Country Sanatorium.

These tests were conducted in the Division of Pulmonary Diseases, Montefiore Hospital for Chronic Diseases, New York, and Bedford Hills, N. Y.

1. The polyvinyl butyral resin used in this experiment was vinylite xysc—purchased by Montefiore Hospital from the Carbide and Carbon Chemical Corporation, New York.

Then tests were carried out in which that basic solution was used with different plasticizers. These tests proved that best results were obtained with the use of castor oil and an organic compound (flexol) as plasticizers.

GROUP I

One hundred and seventy-five male and female patients in the wards of the Pulmonary Division of Montefiore Hospital were used as subjects. Thirty of these patients were known to be sensitive to the customary adhesive plaster. To an area 2 inches (5 cm.) square on the inner side of one forearm of each of the 175 persons, an application of the liquid adhesive was made and allowed to dry. The dried membrane of liquid adhesive was left on the arm for at least twenty-four hours, after which time observations were made. In no case was there redness or any noticeable abnormality of the skin, and none of the patients complained of itching or other discomfort. In order to investigate the possibility of delayed reactions, observations were again made on all the patients a week later, and the results were the same.

GROUP II

Fifty-three male and female patients were the subjects. Nineteen of these had had adhesive plaster burns within the past two years. Of these, 4 patients had adhesive plaster burns on the chest and back at the time of this experiment.

The procedure in this experiment was as follows:

The polyvinyl butyral resin liquid adhesive was applied to a 2 inch (5 cm.) gauze pad of an average of six thicknesses, which was placed on the skin of the subject. Seventeen male subjects had the dressings applied to the back, and 36 male and female patients (21 male and 15 female), to the arm. The dressings were applied in the manner previously described and permitted to remain for twenty-four hours, after which time they were removed, observations were made and new dressings were applied on the other arm and on the other side of the back. These dressings were kept on for twenty-four hours. Observations were made and the process repeated again until a total of twenty-eight to thirty dressings had been applied to each patient.

Thus there were over fifteen hundred dressings applied to 53 patients. All observations were negative except in 3 cases.

CASE 1.—Dressings were applied to the arms of a man daily for seven days with no noticeable reaction. On the seventh day the patient took a bath and left the dressings on. The following day the dressings were removed, and the skin appeared to be red and inflamed. New dressings were applied to the other arm, kept on for twenty-four hours and removed. No redness or other reaction was observed; however, the area covered by the dressing appeared red and inflamed the following day. Another dressing was applied, and the patient was instructed to wet the dressing; several minutes after he had done so, itching began. The dressings were removed, and the area of skin was red and inflamed. Itching lasted several minutes, and redness disappeared in four days.

CASE 2.—After eight days of application of dressings to the back, it was found that there was a slight redness of the skin underneath the dressings. Dressings were repeated at twenty-four hour intervals, and the redness persisted. After the last dressing the redness disappeared within three days and there was no other abnormal cutaneous manifestation.

CASE 3.—After nine repeated dressings at twenty-four hour intervals, a slight redness was observed on the skin underneath the dressings. No other cutaneous abnormalities were observed. Dressings were repeated at twenty-four hour intervals for five more days. Redness persisted under the dressings, and the patient complained of a slight itch while dressings were on. The redness disappeared after three days. No other cutaneous manifestations were observed.

In these cases, after periods of seven, eight and nine days respectively, a slight redness appeared on the skin, accompanied by a minor irritation on the removal of the dressings. After three or four days the symptoms disappeared, and there were no other abnormal cutaneous manifestations.

COMMENT

In all cases the patients expressed the opinion that the polyvinyl butyral resin dressings were more comfortable than the adhesive plaster dressings they were used to, and in all cases dressings were easily removed without any debris remaining on the skin and without use of solvents.

Further experimentation is indicated for the use of solutions of polyvinyl butyral resin for the protection of the skin surrounding draining fistulas, and against the macerating and irritating effects of the exudates. Experimentation is also indicated to determine the advantage of the admixture of specific medicaments with the liquid adhesive used in this experiment.

Brief studies were made of solutions of polyvinyl butyral resin with ethyl cellulose and aluminum dust. These mixtures were applied to the skin surrounding draining fistulas and were found to afford greater protection against the maceration caused by the exudates than was possible by applications of ointments. The use of water-shedding agents, such as aluminum stearate and zinc stearate, aided in protecting the skin.

SUMMARY

A liquid adhesive has been produced which possesses sufficient elasticity and is capable of being applied with ease and removed without leaving any debris on the skin. The fact that 19 patients unable to tolerate the customary adhesive plaster were unaffected by this liquid adhesive, with the possible exception of 3 persons mentioned, gives evidence as to its usefulness as a substitute for adhesive plaster.

370 Cypress Avenue.

PROGRESS IN ORTHOPEDIC SURGERY FOR 1942

A REVIEW PREPARED BY AN EDITORIAL BOARD OF THE AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS

XI. CONDITIONS INVOLVING THE SPINE AND THORAX EXCLUSIVE OF THOSE IN THE LOWER PART OF THE BACK

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(Continued from page 515)

Haas [318] reports a case of spastic scoliosis with obliquity of the pelvis treated by surgical transference of muscle. The patient had considerable pelvic obliquity and a left lumbar scoliosis. The author points out that it is important to obtain a balancing of the muscle pull on both sides of the pelvis and the thoracic cage. He points out that scoliosis with pelvic obliquity due to spastic paralysis is an infrequent entity: "The correction of this deformity is difficult because of the complicated causative mechanical factors, the disorganization of normal muscle control, incoordination, and disturbance in equilibration. It is important that, in attempting a correction of this deformity, one does not further disrupt locomotion by increasing the imbalance or enhance the ability of accommodation for co-existing deformities."

The author considers the possible methods of correction in this type of case. He feels that spinal fusion would have to include the sacrum with the lumbosacral joint and all the lumbar vertebrae. "In view of the bad results obtained with this type of fusion in cases of poliomyelitis, it was thought to be particularly inadvisable in spastic paralysis. A constant strong unilateral pull may cause a return of the deformity with permanent fixation. A spastic patient with disturbance in equilibration may need the free movement of the spine and pelvis to maintain his balance."

[ED. NOTE.—It seems important to stress the point that a spastic patient with disturbance in equilibration may need the free movement of the spine and pelvis to maintain his balance. This is a definite argument against the use of spinal fusion in cases of spastic scoliosis. However, many orthopedic surgeons will not agree with the author regarding the bad results obtained with fusion in cases of poliomyelitis, and it should be pointed out that some surgeons have had excellent results. The results following fusion in cases of poliomyelitis depend considerably on such factors as the technic used and the type of correction.]

The author discusses the use of a strut graft from the ilium, which he considers inadvisable. He also discusses the release of the sacrospinalis, lateral abdominal, anterior abdominal and quadratus lumborum muscles, which would entail an extensive dissection, a difficult problem of balance of pull and the possibility of herniation and other bad sequelae. Neurectomies or other nerve-destroying operations on the involved muscles are not considered advisable. The author also mentions that fascial slings or checks from the ribs to the pelvis on the opposite side, such as have been used in poliomyelitis, may be successful. The opposing strong constant pull would tend to stretch the fascia unless a compensatory hypertrophy took place. There is also the difficulty of completely fixing one half of the pelvis.

The author points out that the greater pull of the spastic muscles on the right side over the normal pull of the muscles of the left side was considered to be

318. Haas, S. L.: Spastic Scoliosis and Obliquity of Pelvis, J. Bone & Joint Surg. **24**:774-780 (Oct.) 1942.

responsible for the scoliosis and the obliquity of the pelvis. If some of the pull of the anterior and posterior muscles could be transferred to the opposite side and the correct balance obtained, the deformity could be permanently corrected. As it could be actively corrected by the use of the Carl Jones splint, it was known that no permanent structural changes had taken place. If the method did not work, then some of the other methods could be utilized to supply any deficiency. The author then describes the two operations by which he transfers the pull of the external oblique and rectus abdominis muscles and also the pull of the latissimus dorsi and longissimus dorsi muscles, by use of fascial strips and transfer of muscle. He points out that it is possible that the same type of correction could be secured in early paralytic scoliosis before fixed contracture and structural changes had occurred in the vertebrae. "It would be necessary to know definitely which groups of muscles are involved before any muscle transference operation could be performed. Unfortunately it is not easy to determine this fact in many cases of scoliosis."

[ED. NOTE.—It should be stressed here that it is not easy to determine which group of muscles is involved in most cases of paralytic scoliosis. Also paralytic scoliosis frequently stops increasing and does not progress beyond the early stage, so that many unnecessary operations might be done. The author concludes that "transference of muscles in association with fusion operations may help to reduce the loss of correction and the tendency to recurrences following fusion operations for scoliosis of the spine." While marked muscular imbalance may cause a loss of some correction following spinal fusion in some cases of paralytic scoliosis, usually the loss of correction and the tendency to recurrence following fusion are due to the fact that the fusion is not adequately performed and completely solid, with an amount of bone adequate to hold the trunk mass. When the fusion is adequately done with a sufficiently large amount of bone, even pronounced muscle imbalance can often be overcome. The curvature frequently does not increase, and often most of the correction can be maintained.]

Wenger [319] in an article on rib resection in the treatment of scoliosis reviews the material previously reported in a paper by Wenger and Herman entitled "The Role of the Transverse Process in Thoracogenic Scoliosis" which was reviewed in "Progress in Orthopedic Surgery for 1941." He discusses the material presented in the previous article but draws other conclusions. The author states:

> Analysis shows the following facts:
>
> 1. In the majority of the cases there was convexity of the spine toward the operative side.
>
> 2. The number and the length of the costal segments resected do not of themselves alter the resulting scoliosis.
>
> 3. In all cases in which there was marked convexity to the side on which operation had been performed either the transverse process was injured or the anterior costotransverse ligament was cut. In cases in which the transverse processes were left intact, slight curvature or none at all resulted.
>
> 4. In all the cases (3.5 per cent) in which the patients were children there was destruction of the transverse processes. This possibility explains the severe postoperative curvature.
>
> 5. Resecting a larger number of ribs does not necessarily increase the curvature. However, if a transverse process is injured or removed the curvature occurs.
>
> 6. Resection lateral to the angles of the ribs causes practically no deviation except in children.
>
> 7. There are no sharply angulated curves; that is, there are no wedged vertebrae. (All are C curves.)

319. Wenger, H. L.: Rib Resection in Treatment of Scoliosis, Arch. Surg. **44**:119-128 (Jan.) 1942.

8. As successive rib resections are carried out at lower levels, the apex of the curve descends.

9. Mediastinal displacement does not necessarily cause scoliosis.

10. There was no change in spinal curvature in 7 cases in which basal thoracoplasty was performed. Apparently basal thoracoplasty has little effect on the spine.

11. In cases in which successive ribs are removed and at one point a transverse process is resected, the apex of curve suddenly localizes at that point, and the curve increases.

12. Regeneration of ribs will prevent scoliosis.

13. In all cases the resulting curve averaged 18 degrees.

He concludes that scoliosis due to thoracoplasty results from trauma or removal of the transverse processes and that rib resection of itself has little, if any, influence in causing the condition. "On the basis of these findings transversectomy to correct primary scoliosis is now being done on the concave side of the spinal curvature."

[ED. NOTE.—It seems obvious that the cause of scoliosis following thoracoplasty is a disturbance of the bone-muscle mechanism supporting the spine. The ribs and their muscular attachments have a definite mechanical effect on the position of the spine. One of Wenger's patients had practically no scoliosis after resection of ribs on both sides. It is obvious that this would be true even if the transverse processes were resected. It is also obvious that the curvature is likely to be more deforming and more severe if there is great damage to the bone and muscle balance.

Therefore one would assume that resecting the transverse processes as well as the ribs would add to the instability. However, there are definite known cases of curvature, especially in children, in which the curvature developed following resection of ribs only. His series has only 9 children (3.5 per cent). This is a very small series, and he does not state how long they were followed nor how severe the curvatures were. He reports that the average resulting curve was 18 degrees. This is not a severe curve and does not require any treatment for the curvature itself, especially in adults. The serious part of the problem of scoliosis following thoracoplasty relates to the children whose later growth adds to the deforming factor. Most adults with scoliosis following thoracoplasty do not have severe curves and do not require much, if any, treatment for the curvature.

The author states that resection lateral to the angle of the ribs causes practically no deviation except in children. In many of the cases with only partial rib resection a small area is done, and in these patients such a severe scoliosis would not be expected to develop. Also, he does not explain why there is no deviation except in children. Why should scoliosis develop in the children if the transverse process were the only cause? It is obvious that if thoracoplasty on the left will cause a curvature of the spine convex to the left, such a procedure carried out in a child having a scoliosis convex to the right will result in a type of scoliosis likely to counteract the original tendency. However, thoracoplasty on the concave side of an idiopathic curve is an extremely drastic procedure. There is already beginning decreased vital capacity on the right side, which is the side of the convexity, and in performing a thoracoplasty on the left, one would have to remove sufficient ribs to decrease the vital capacity on the left as well as on the right. While mechanically this might seem worth a trial, clinically, considering the physiology of the patient, it seems entirely too radical a procedure.

Dr. Wenger states that he is doing a transversectomy on the concave side to attempt to correct scoliosis due to other causes, including idiopathic scoliosis. He does not note that in addition to resection of the transverse processes the patients

in this series also had resection of the ribs on the convex side. In other words, he has not established the fact that if the transverse processes alone are resected scoliosis will develop. He has merely shown that scoliosis develops after rib resection and resection of the transverse processes. It has yet to be shown whether resection of the transverse processes alone could cause scoliosis. It should also be pointed out that in probably 80 per cent or more of cases of so-called idiopathic scoliosis the deformity stops progressing when the curve is not severe enough to require any radical treatment. It would be necessary to do the resection of the transverse processes while the curve was very slight, in order to get any beneficial effect. It would therefore be easy to find a large series of cases in which the curve did not increase after resection of the transverse processes because in a large percentage it would not increase anyway. It would be difficult to prove that resection of the transverse processes actually was the cause of stopping the progressing scoliosis. The report of Dr. Wenger's cases in which he has done resection of the transverse processes for the treatment of scoliosis will be awaited with interest.]

Martin [320] reports 4 cases of atloaxoid dislocation following cervical infection. He points out that while dislocation of the atlas on the axis is often traumatic, with fracture of the odontoid process and resultant damage to the cord, it may also occur as a sequel to cervical infections. This second cause brings the patient into the field of the otorhinolaryngologist, who deals with infections in this region and who must recognize the source of the dislocation. He feels that the best explanation of the pathologic changes which occur is that of Greig [321]:

> . . . cervical infections, by producing hyperemia, cause vertebral decalcification of a greater or less degree. The ligaments are so strong that they cannot be avulsed without tearing off fragments of bone with them, but if the bone has undergone previous decalcification the ligaments yield readily.
>
> Jones demonstrated this decalcification in some of his roentgen studies. He showed that it is peculiar to children at an age when the bones are imperfectly developed and not well calcified, that an inflammatory lesion anywhere in the upper cervical region may cause such decalcification; that the anterior arch of the atlas may show decalcification without destruction and, finally, that the onset of dislocation usually occurs about ten days after the infection begins.

Evidently Desfosses and Grisel believed that nasopharyngitis causes muscle spasm which produces the torticollis and vertebral subluxation, but Greig disagreed, asserting that the spasm of the prevertebral and occipitovertebral muscles splints the bones and is therefore a result, not a cause. These authorities gave the following sequence of events:

> . . . (1) cervical infection with hyperemia, (2) vertebral decalcification and loosening of the ligamentous attachments, (3) slipping forward of one or both lateral articular facets of the atlas and locking as the facet slips forward and downward over the opposing facet of the axis, or (4) slipping backward of one articular facet of the atlas (if both lateral facets slip to any degree death may supervene since to permit this to happen the odontoid must have moved posteriorly and thus have crushed the cord). Berkheiser and Seidler presented 2 such cases in a series of 5, but they overlooked the fact that in any three-point suspension two points must always move, otherwise a fracture occurs.

The author points out that the patient holds his head rigidly, slightly in front of the normal plane tilted toward one shoulder with the face rotated toward the opposite shoulder. Tenderness over the lateral masses of the axis and atlas occurred

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320. Martin, R. C.: Atlas-Axis Dislocation Following Cervical Infection, J. A. M. A. **118**:874-875 (March 14) 1942.

321. Greig, D. M.: The Surgical Pathology of Bone, London, Oliver & Boyd, 1931.

in all 4 of his cases. There is no spasm of the sternomastoid muscle such as occurs in "spastic" torticollis, the rigidity resulting from spasm of the deep cervical muscles. He says:

> One may see an occasional case of torticollis preceding or following mastoidectomy and must be alert not to attribute it to an unconscious attempt on the part of the patient to relax an inflamed sternomastoid muscle on the diseased or operated side. Two of our patients whose dislocation was associated with mastoiditis, one occurring before operation and the other after operation, held the head tilted toward the sound side and the chin toward the diseased side. This position actually increased the strain on the inflamed muscle and caused me to consider the possibility that a cervical dislocation had in fact occurred.
>
> It should be emphasized that care must be exercised in placing a patient for operation and in moving him postoperatively, particularly after severe or long-lasting cervical infections. In 1 case in our series (case 4) in which the dislocation was found after operation, the position on the table may have been partly responsible for the dislocation by stretching of the ligamentous attachments, though the dislocation did not occur until twenty-four hours after operation.

Two dislocations subsequent to tonsillectomy and 1 subsequent to local anesthesia have been reported. In another case there was gradual onset of dislocation for two weeks after an adenotonsillectomy. No neurologic signs or symptoms were present in any of the 4 cases; so there was no compression of the cord. The author accomplished reduction of the dislocation by accentuating the deformity in addition to traction, permitting unlocking of the lips of the lateral articular facets. Reposition of the vertebrae is secured by extension and by bringing the head to the midline while rotating the chin to its normal position. Fixation in plaster for a variable time allows healing and reattachment of the ligament. In 1 case a paper collar support was used after removal of the plaster. The results in all cases were good.

[ED. NOTE.—While atlas-axis dislocation following cervical infections have been previously reported, this article covers the problem well and again calls attention to the importance of not overlooking possible association of atlas-axis dislocations with cervical infections. Some later and prolonged orthopedic problems concerning the neck may be related to some of these conditions which have been neglected.]

Hess, Abelson and Bronstein [322] present a case of unreduced spontaneous atlantoaxial dislocation and suggest that this condition should be looked for in cases of unexplained kyphosis and scoliosis. They bring up the question whether unreduced atlantoaxial dislocation may play a role in the production of certain orthopedic conditions, such as wry neck, scoliosis and cervical arthritis. They report a case in which treatment was not given in which the dislocation persisted after a period of five years. They point out the importance of careful follow-up in the treatment of infectious diseases and of suppurative conditions about the head and neck in order to avoid this complication.

[ED. NOTE.—This condition has been previously reported, and in most cases simple traction with or without manipulation seems to be sufficient. Careful follow-up, including roentgenograms, is important.]

Weiler [323] reports another case of congenital absence of the odontoid process of the second cervical vertebra or epistropheus, resulting in atlantoepistropheal dislocation. Fusion following reduction was successful. The patient has no symptoms after two years. Weiler briefly reviews the history of the subject as

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322. Hess, J. H.; Abelson, S. M., and Bronstein, I. P.: Spontaneous Atlantoaxial Dislocations; Possible Relation to Deformity of Spine, Am. J. Dis. Child. **64**:51-54 (July) 1942.

323. Weiler, H. G.: Congenital Absence of Odontoid Process of Axis with Atlanto-Axial Dislocation, J. Bone & Joint Surg. **24**:161-165 (Jan.) 1942.

reported in the literature and points out that the dislocation may be reduced by continuous cervical traction or manipulation but that reduction of the dislocation appears insufficient unless fixation of the atlas is made to the axis to prevent recurrent slipping. For fusion the author used a short section of rib, split longitudinally and sutured to the first and the second cervical vertebra. In this case manipulation with the patient under cyclopropane anesthesia was necessary for reduction. The operation was done on the atlantoaxial area through a window in the back of the cast.

[ED. NOTE.—The congenital absence of the odontoid process of the axis with dislocation is relatively rare and is therefore worth mentioning in the review of the literature. It might also be pointed out that in most cases in which operation on the high cervical area is required, especially where there is a question of dislocation and mechanical instability with resultant danger of collapse during the operation, it is usually considered safer to perform the operation with traction on the skull rather than through a plaster. The operation has been done with plaster and with traction, and it has been done without either. Most surgeons feel that the operation is safer with the patient under skeletal traction with either tongs or wires in the skull.]

Jostes [324] reports 9 cases in which laminagrams of the cervical vertebrae were an aid in diagnosis of occipitocervical lesions. He discusses the various conditions causing pain in the neck or occipital region with radiation toward one or both shoulders and the treatment for these cases, especially stressing the aid obtained by use of the laminagram.

[ED. NOTE.—Ordinary roentgenograms of the cervical vertebrae are frequently difficult to interpret, and the laminagram evidently should be used more extensively in these cases. Probably many patients whose pain is routinely relieved by such measures as traction on the head, immobilization and the wearing of a leather collar would fall into the class reported by Dr. Jostes if a laminagram had been taken and a more definitely localized diagnosis made.]

Craig, Walsh and Camp [325] report on 3 patients with the roentgenographic picture of basilar invagination of the skull. In 2 of the cases associated anomalies of the upper cervical vertebrae also were present. In all 3 cases the clinical symptoms suggested involvement of the spinal cord in the upper cervical region and the brain stem, whereas the neurologic signs indicated a lesion of the cerebellum or its tracts. There was 1 case each of a lesion of the brain stem and a lesion of the spinal cord in the upper cervical region. Marked respiratory difficulty occurred in 1 case. In all 3 cases adhesions between the meninges and inferior poles of the cerebellar lobes and brain stem were noted at operation and freed. In 2 cases marked herniation of portions of the cerebellar lobes occurred. Relief from symptoms was striking in all cases.

The authors also point out that a characteristic roentgenographic picture of basilar invagination of the skull has been encountered among several patients who had neither clinical symptoms nor signs of involvement of the nervous system.

[ED. NOTE.—While previous cases of invagination of the skull have been reported in which improvement followed operation, this paper seems worth mentioning, for, as the authors point out, "Now that we are aware that 'platybasia' or

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324. Jostes, F. A.: Neck Pain: Laminagraph as Aid to Diagnosis of Atlanto-Occipital Lesions, J. A. M. A. **118**:353-359 (Jan. 31) 1942.

325. Craig, W. M.; Walsh, M. N., and Camp, J. D.: Basilar Invagination of Skull—So-Called Platybasia: Report of Three Cases in Which Operation Was Done, Surg., Gynec. & Obst. **74**:751-754 (March) 1942.

more nearly accurately, basilar invagination of the skull, is a deformity of the occipital bone, which narrows the foramen magnum, and of the upper cervical vertebrae, which flattens the spinal canal and that removal of the bone which is compressing the underlying brain and spinal cord usually will be followed by relief of symptoms, the syndrome is receiving more recognition." Like many other obscure problems and syndromes, this condition will be frequently overlooked until it becomes better known by constant report of cases.]

Haynes [326] reports a case of dural constricting ring with cervical protruded intervertebral disk. A severe arachnoid and dural reaction at the foramen magnum was interpreted as being secondary to a space-occupying lesion of the cervical portion of the spinal cord, in this case a protruded intervertebral disk.

> In the absence of platybasia or other bony deformity, a dural and arachnoid constricting ring was found at the level of the foramen magnum, the reaction apparently starting at the level of the protruded intervertebral disk at the fifth cervical vertebra and extending cephalad, becoming very marked at the foramen.
>
> It is suggested that, contrary to general opinion, the syringomyelic cavity below a dural constricting ring at the foramen magnum is not secondary to the malformation, but causes the dural and arachnoid reaction resulting in the malformation.
>
> This report does not attempt to explain the syringomyelic cavity found in the cases of platybasia where the odontoid process has caused a dural reaction resulting in the same constricting ring.

This is an interesting report, and, as the author points out, the case tends to favor the belief of Hassin "that a long standing or advanced syringomyelic cavity or other space-occupying lesion of the cervical cord might cause meningeal changes." In this case the space-occupying lesion at the level of the fifth cervical vertebra was not a syringomyelic cyst but a protruded intervertebral disk. This lesion was accompanied by an arachnoid reaction, which surrounded it, extended upward and culminated in severe arachnoid proliferation, dural thickening and the formation of a dural constricting ring at the level of the foramen magnum. "Complete roentgenographic studies revealed no evidence of platybasia or upper cervical malformation and none was found at the time of operation."

[ED. NOTE.—This interesting case is well worth reporting and seems to contribute further to the knowledge of some of the rare and difficult conditions involving the upper cervical areas of the spine.]

Brown and Kuhns [327] state:

> The symptoms commonly found in the so-called scalenus syndrome and in cervical ribs may be caused by remote factors as well as local ones. The symptoms are frequently due to trauma, either from a definite strain or from the chronic strains which come in the use of the whole body, and especially of the chest and cervical spine, for a long period of time in faulty mechanics, combined with general relaxation and fatigue. In the authors' experience, the correction of the extension deformity of the cervical spine, combined with the correction of the faulty use of the body as a whole will bring relief of the neurological as well as of the vascular symptoms, in the majority of cases, without the necessity of operative procedures.

They also point out that

> . . . the distribution of the symptoms will depend among other factors, upon the location of the habitual position of extreme extension of the cervical spine. If the apex of the curve is in the upper cervical region the distribution will be through the cervical nerve plexus; and, if in the lower cervical spine, the distribution will be through the brachial plexus.

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326. Haynes, W. G.: Dural Constricting Ring with Cervical Protruded Intervertebral Disk: Report of Case, New England J. Med. **227**:825-827 (Nov. 26) 1942.

327. Brown, L. T., and Kuhns, J. G.: Extension Deformities of Cervical Spine, J. Bone & Joint Surg. **24**:329-340 (April) 1942.

Aynesworth describes the scalenus and cervical-rib syndrome in the inclusive term cervical-brachial syndrome, and divides the cases into three groups: (1) those which exhibit neurological symptoms as their chief manifestation; (2) those which exhibit vascular symptoms as their major manifestation; and (3) those which exhibit a combination of vascular and neurological symptoms. This suggests the probability that there must be causes more widespread and remote than the usual explanation of local pressure from a thickened scalenus anterior or a cervical rib.

They describe the anatomy of the cervical vertebrae and give details of their treatment for extension deformities.

The object of treatment is to correct the extension deformities in the cervical and lumbar regions of the spine, and also the flexion deformity of the thoracic spine and the associated drooped chest. The correction of the extension deformity of the cervical spine is most easily accomplished by recumbency on the back on a firm mattress. To relieve the strain on the lumbar spine, a large pillow under the knees and a small pillow to fill the hollow in the low back is helpful. With this procedure muscle spasm subsides quickly in most instances. The authors have rarely found head-traction necessary. A felt collar, fitted low in front and high in back, to reduce the extension deformity, adds to the patient's comfort. The correction of the drooped chest and of the extension deformity of the lumbar spine is obtained gradually by exercises planned to correct the habitual faulty position of use. These are begun in recumbency and progress to the sitting and standing position, emphasis being laid upon good body mechanics rather than upon the exercises *per se*. When the ambulatory stage is reached, support for the spine and abdomen is usually necessary.

[ED. NOTE.—This is a good paper on symptoms referable to the cervical area, frequently seen in orthopedic surgery. The authors point out that occasionally operative treatment may be required and tend to confirm the view of many other orthopedic surgeons who have had success in the relief of scalenus anticus and cervical rib syndromes by conservative methods and without operation. It has been pointed out by others previously that probably 80 per cent or more of patients with the scalenus anticus or cervical rib syndrome can be relieved without operation, and it seems worth while to stress the conservative treatment. It is likely that many patients who have had operations for the scalenus anticus or cervical rib syndrome could have been relieved by conservative methods.]

Haggart and Toumey [328] describe a method of spinal fusion which is a modification of the Hibbs procedure and in their hands has proved a most satisfactory technic. They describe the usual technic for exposure of the spine in the area to be fused and emphasize the importance of curetting the articular facets, stressing the point that it is important to obtain fusion.

[ED. NOTE.—There are a great many orthopedic surgeons who do not feel it is necessary to obtain fusion of the articular facets if a proper spinal fusion is done. Incidentally, the articular facets frequently will disappear after a period of years, even though they were not disturbed at the time of operation. The technic described by these authors is essentially a modification of the Hibbs technic with some variation in turning up and down the flaps or chips of bone from the laminas and in addition adding bone from the ilium. It should be noted that when the spinal fusion is performed through a hole in the plaster jacket, as is so frequently done, during the correction for scoliosis it is difficult or impossible to obtain bone from the ilium and therefore usually necessary to use tibial bone. It is also very likely that more bone and better osteoperiosteal strips can be obtained from the tibia. It should be noted that these authors still use the original procedure of removing the spinous processes entirely and making bone chips of them. Turning these chips up and down from the spinous processes without removing them is

328. Haggart, G. E., and Toumey, J. W.: Spine Fusion: Effective Technique, S. Clin. North America **22**:873-881 (June) 1942.

preferred by many surgeons. The authors conclude that "meticulous attention to the details noted herein will result in a consistently firm fusion in the region operated on, as shown in the postoperative roentgenogram, which exhibits a large mass of bone that completely stabilizes the lumbosacral spine." This conclusion seems rather optimistic, since there is no method of spinal fusion which is 100 per cent successful in any one's hands. Incidentally, the reproductions of the roentgenograms are rather poor, and it is difficult to see the large mass of bone that they describe, at least in these reproductions.]

Crawford [329] describes a method of extensive laminectomy with replacement of removed laminas. He says:

> The easily approachable sharply localized protruded masses from ruptured intervertebral discs can often be adequately removed with minimal or no bone removal. This has the advantage of prompt convalescence and little or no weakening of the back.
>
> In my experience there are some cases with good clinical history and findings of ruptured discs which at operation have shown neither a ruptured disc nor a thickened ligamentum flavum, but where the cause of nerve impingement has been one or more of the following anatomic structures: (1) The upper lip of the fifth lumbar facet, with a relaxed joint, associated with increased lumbosacral lordosis; (2) Hypertrophic arthritis resulting in a flaring out of the borders of the vertebral bodies, thus simulating a prominent intervertebral disc; (3) A structurally small intervertebral foramen due to bony changes or to increased tissue, including dilated lumbar veins, surrounding the nerves in the foramina.
>
> Clinically these cases are similar to those due to ruptured discs, but are less likely to have clear-cut traumatic histories, usually have a more prolonged and intermittent course and although they may have improved with conservative therapy, have had repeated recurrences of pain and finally have become incapacitated. They may have bilateral signs or symptoms which may involve either or both of the fourth and fifth lumbar nerves.
>
> To adequately expose these nerves on both sides by the usual method of laminectomy with rongeurs may leave a structurally weak back, as the facets may have to be removed.
>
> In attempting to meet this latter problem, lately we have been removing in one piece with chisel and mallet, the entire dorsal arch composed of a spine, lamina, and attached facets. [ED. NOTE.—This procedure gives an excellent exposure of both nerves throughout their entire course through the foramina.] Sometimes we have had to chisel off the overhanging edge of the facet to free up an adherent involved nerve. At times enlarged veins accompanying the nerve through the foramina, appear to be an important etiologic factor.
>
> After the nerves have thus been adequately decompressed and the removed bone fragment trimmed up so it cannot itself later cause nerve impingement and the cartilage of the facets has been scraped off to insure bony ankylosis, the piece is then returned to its bed and sutured in place with silver or stainless steel wire between the adjacent spines and facets. The patient is kept on a Bradford frame for a few days and then has a back brace fitted to be worn until the graft is safely grown in place.

The author states that this operation had been done on 7 patients during the ten months preceding the writing of his article, and thus far had proved to be satisfactory. It had given excellent exposure for thorough decompression without the weak backs which almost certainly would have resulted from the use of the old method. Also, the patients had been able to return to active work sooner than they would have with tibial bone grafts.

[ED. NOTE.—As the author points out, this is too small a group of cases to serve as a reliable guide, and more time should pass to see whether any unfavorable after-effects might develop. He does not advocate its use when the lesion is certainly unilateral and when it can be adequately relieved with a hemilaminectomy. It should be mentioned that the removal of this portion of the spine produces in effect a spondylolysis or prespondylolisthesis and creates the same mechanical situation found in prespondylolisthesis, in which the fifth lumbar body may slide

329. Crawford, A. S.: Method of Extensive Laminectomy with Replacement of Removed Laminae, Surgery **12**:482-485 (Sept.) 1942.

forward on the sacrum. This extensive removal of bone might possibly add further complications by causing a spondylolisthesis, and the only thing to prevent this is a fusion between the denuded articular facets and the osteotomized pedicles when the large fragment is replaced. Also, following this procedure it is questionable whether there is sufficient assurance of fusion to warrant letting the patient up any sooner than one would after any operation for spinal fusion. The incidence of pseudarthrosis following lumbosacral fusions is high, and after this procedure the same problems of bone healing would be present. This method certainly gives an excellent exposure, but when it is indicated one may find that spinal fusion with additional bone and more immobilization is required to prevent recurrent symptoms. The use of the Wilson type spine plate with bolts through the spinous process (when there is an adequate first sacral spinous process) seems to present definite advantages for obtaining early adequate immobilization of the fusion area and with adequate spinal fusion, including additional bone, is giving very excellent results.]

Horwitz [330] calls attention to a painful deformity observed in the lumbar region of the spine in 3 cases and in the dorsal region of the spine in 1 case following bilateral laminectomy. These patients returned for observation from eight months to fifteen years after bilateral laminectomy involving from two to five vertebrae in which the spinous processes and the laminas on both sides had been removed but the articular facets had been preserved.

> They complained of a variable amount of pain, weakness and fatigue in the back, and they presented obvious deformity associated with changes in the intervertebral discs and vertebral bodies in the region of the laminectomy. A similar deformity has been reported by Taylor following bilateral laminectomy in the cervical spine.
>
> . . . Only 5 cases out of 25 bilateral laminectomies were available for study. Four of these 5 cases demonstrated the painful spinal deformity herein described. The fifth patient was as yet asymptomatic.

The author points out:

> The use of immediate or delayed spine fusion following laminectomy in the absence of a weakened or diseased vertebral column, has been considered unnecessary by most neurosurgeons. However, an increasing number of orthopedic surgeons are favoring the use of spine fusion in conjunction with the laminectomy.

Horwitz believes that one of the indications for immediate spinal fusion following bilateral laminectomy, the patient's condition permitting, is the prevention of such symptomatic deformities as have been reported by Taylor in the cervical portion of the spine, and in the cases presented. He also feels it is important for patients who are subjected to bilateral laminectomy without immediate spinal fusion to have periodic roentgenograms of the spine in order to ascertain the development of spinal deformity and of secondary changes in bone and soft tissue. He points out that delayed spinal fusion in such cases is technically more difficult than fusion performed at the time of laminectomy and that the vertebral changes which have developed are permanent.

It is possible that hemilaminectomy, as recommended by Taylor, partial laminectomy with preservation of the neural arch, as recommended by Love and Walsh, and the interlaminar approach of Love may obviate the need for spinal fusion, but the use of these procedures, especially of the latter two, is restricted because of their limited exposures. Horwitz points out that symptomatic spinal deformity may appear and preexisting spinal deformity may become aggravated following

330. Horwitz, T.: Structural Deformities of the Spine Following Bilateral Laminectomy, Am. J. Roentgenol. **46**:836-840 (Dec.) 1941.

bilateral laminectomy in the cervical, thoracic and lumbar regions of the spine, even when the articular facets are preserved. He suggests that such deformities may be prevented by spinal fusion. In cases in which immediate fusion is not done periodic roentgenography is advised for the early diagnosis of secondary changes, and for these he advises fixation by spinal fusion or external fixation.

[ED. NOTE.—As the author points out, an increasing number of orthopedic surgeons are favoring the use of spinal fusion in conjunction with total laminectomy. This operation obviously does weaken the structural elements of the posterior part of the spine, especially in heavy patients or in patients engaged in heavy labor. It certainly is easier to do the spinal fusion immediately after the laminectomy than to do it at a later date. Probably the recurrent symptoms of many of the patients who have undergone laminectomy are caused by structural weakness due to the operation rather than by the original lesion.

It will be interesting to have further reports on other total laminectomies to determine the relative incidence of symptoms as reported in this paper. Probably the onset of symptoms will depend on a number of factors, including the initial lesion requiring bilateral laminectomy (which may well have been an involvement of the disk), other preexisting instabilities or pathologic processes, the weight of the patient and the type of occupation.]

Everett [331] reports 3 more cases of injury to the intervertebral disk following lumbar puncture. While this condition has been previously recorded, he stresses this as an important complication following lumbar puncture. Roentgenograms showed definite narrowing of the previously normal intervertebral space at the level where the lumbar puncture was done.

[ED. NOTE.—While this condition has been previously reported, it may be well to stress it as a complication which should be considered in doing routine lumbar punctures.]

Epps [332] also reports a case of degeneration of the intervertebral disk following the lumbar puncture. Roentgenograms showed definite collapse of the intervertebral disk. The process appeared to be an aseptic degeneration. This is a short article and merely reports another case.

Simon [333] points out that since neither healing nor prevention of the pronounced and fixed kyphosis in kyphosis dorsalis juvenilis is possible except in the primary stage of the disease, an early diagnosis is of the utmost importance. He states that most authors have observed the disease in patients between the ages of 15 and 22 years, while some of his were observed much earlier in the disease.

Following the theory of Schneider that there is some relationship between the diseases of the epiphysis and vitamin-A deficiency, the eyes of all the children were examined for hemeralopia and zerophthalmia. It was found that most of the children with kyphosis dorsalis juvenilis suffered from slight hemeralopia, and xerophthalmia was found in two of the group from nine to thirteen years of age. In a parallel group of children with poor posture only practically no hemeralopia and no child with xerophthalmia was found.

The blood serum of these children was examined for carotene beta and vitamin A, and it was found that most of the children with kyphosis dorsalis juvenilis showed a lack or deficiency of vitamin A. In the blood-serum test for vitamin A the average for the younger group with kyphosis dorsalis juvenilis was 5 international units, and for the older group 130; the average for the total group with poor posture only was 85 international units (without essential dif-

331. Everett, A. D.: Lumbar Puncture Injuries, Proc. Roy. Soc. Med. **35**:208-210 (Jan.) 1942.

332. Epps, P. G.: Case of Degeneration of Intervertebral Disc Following Lumbar Puncture, Proc. Roy. Soc. Med. **35**:220-221 (Jan.) 1942.

333. Simon, R. S.: Diagnosis and Treatment of Kyphosis Dorsalis Juvenilis (Scheuermann's Kyphosis) in Early Stage, J. Bone & Joint Surg. **24**:681-683 (July) 1942.

ference between the younger and older children). In the test for carotene beta, the average for the younger group of those with kyphosis dorsalis juvenilis was found to be 0.039 milligrams per 100 cubic centimeters of blood serum, and for the older group, 0.046; the average for the total group of those with poor posture only was 0.033.

Since roentgenographic examination of such young patients never shows the pronounced symptoms of the disease, the proof of vitamin-A deficiency is an important aid for early diagnosis. Moreover, if vitamin-A deficiency exists in older patients it demonstrates that the active period of the disease has not passed.

Treatment of kyphosis dorsalis juvenilis in the early stage is based primarily on rest for the diseased spine. This is achieved by a plaster-of-Paris corset, which is worn for six months; wearing this corset, it is possible for the child to attend school. In addition, the child is given 40,000 international units of vitamin A daily for three months.

CONCLUSIONS

1. Kyphosis dorsalis juvenilis (Scheuermann's kyphosis) may be seen between the ages of fifteen and twenty-two years, but it may begin as early as eight or ten.

2. Proof of vitamin-A deficiency is an important supplementary aid in the early diagnosis of the disease.

3. Vitamin-A deficiency in older patients is a probable sign that the disease is still active.

4. Children in the early stage of the disease should be excluded from physical exercises, should be given vitamin A, and should wear plaster-of-Paris corsets.

[ED. NOTE.—While vitamin A deficiency may be a factor in the development of kyphosis dorsalis juvenilis, it should be pointed out that this deficiency may be only a concomitant occurrence and not the causative factor in this condition. The possibility that deficiency of other substances, such as vitamin D and gonadal or endocrine factors, is important in this condition must still be considered.]

Rees and Murphy[334] believe with Scott that spondylitis adolescens is an inflammatory arthritis of the spine of infective origin and that the Marie-Strümpell syndrome, Bechterew's spondylitis and *spondylose rhizomélique* may be classified under the term spondylitis adolescens. They point out its common occurrence and discuss the pathologic change, roentgenographic appearance, symptoms, differential diagnosis and roentgenotherapy. They report 7 cases in which it was treated by roentgenotherapy with definite improvement. The patients were 18, 23, 24, 34, 16, 24 and 28 years old respectively. Rees and Murphy conclude that the earlier the patient is treated in the course of the disease the better will be the result obtained with roentgenotherapy, particularly if treatment can be given in the prespondylitic period. They also suggest that the patient should be hospitalized for roentgenotherapy, as it would otherwise require considerable travel with additional trauma. They also advise that the treatments be taken regularly, approximately twice a week. A table indicating locations and dosages for roentgen treatment is included.

[ED. NOTE.—The conclusions seem to agree with those of most authors who have reported on roentgenotherapy for spondylitis.]

XII. CONDITIONS INVOLVING THE LOWER PART OF THE BACK

PREPARED BY FREMONT A. CHANDLER, M.D., CHICAGO

Papers on pain in the lower part of the back and sciatica published during the past year again emphasize the importance of the herniated intervertebral disk. Experience with this entity is mounting, and the clinical picture is becoming more

334. Rees, S. E., and Murphy, W.: Roentgenotherapy of Spondylitis Adolescens, Northwest Med. **41**:164-166 (May) 1942.

clearly defined. According to Dandy,[335] a history of pain low in the back with sciatica which is accentuated by coughing or sneezing is almost pathognomonic of a ruptured disk, and all other refinements of diagnosis are unnecessary. Even the physical examination may be dispensed with. He points to the fact that he found the ruptured disk in 349 of 350 cases. The single patient whose disease was misdiagnosed had a tumor of the spinal cord. [ED. NOTE.—A follow-up study of this remarkable series should be forthcoming, for it is possible that other surgeons have seen some of the patients subsequently and might add items of interest.] Dandy curets the cavity left by the removal of the disk. He considers fusion unnecessary.

In another paper [336] Dandy stresses the serious sequelae resulting from delay in operative treatment. Cases of pressure necrosis of the cervical cord and subsequent death, permanent paralysis from extrusion of a disk in the thoracic region, and permanent sensory and motor damage with continued sciatica and impairment of vesical function from herniation in the lumbar portion of the spine are reviewed. He concedes that iodized oil is of advantage when there is involvement of the spinal cord. The use of such contrast mediums is not indicated for rupture of a lumbar disk, because with rare exceptions the diagnosis can be made with more accuracy and certainty without it.

Craig [337] states that intermittent attacks of pain are considered an outstanding diagnostic point in the history of patients with protruded intervertebral disks. Paresis was found in 20 per cent of the cases from the Mayo clinic, sensory loss in 18 per cent and no neurologic changes in 8 per cent. Increase of pain on coughing or sneezing was found in 67 per cent. The achilles tendon reflex was lost or diminished in 63 per cent of the patients who had lesions of disks at the lumbosacral junction, in 37 per cent of those with lesions at the fourth interspace and in 52 per cent of those with lesions at the third interspace. The patellar reflex was reduced or absent in 49 per cent of the patients with lesions at the third interspace, in 20 per cent of those with lesions at the fourth interspace, and in 9 per cent of those with lesions at the lumbosacral junction. The total protein content of the spinal fluid was over 40 mg. per hundred cubic centimeters in 61 per cent of the cases. Craig favors roentgen examination with air as a contrast medium and considers a small hemilaminectomy the most suitable operation. Statistics from the Mayo Clinic show that an increasing number of spinal fusions are being carried out along with the laminectomy. The percentage of cures subsequent to operation is definitely higher in the group of patients to whom compensation was not available. The fusion operation should probably be done when there is spondylolisthesis or spondylolysis, congenital deformity or hypertrophic arthritis. Narrowing of the interspace alone is not considered an indication for adding fusion to laminectomy.

Kaplan, Bender and Sapirstein [338] report 4 cases of tumor of the cauda equina in which neurologic signs were absent and unilateral sciatica was the only symptom. They find that myelography is essential for diagnosis.

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335. Dandy, W. E.: Recent Advances in Diagnosis and Treatment of Ruptured Intervertebral Disks, Ann. Surg. **115**:514-520 (April) 1942.

336. Dandy, W. E.: Serious Complications of Ruptured Intervertebral Disks, J. A. M. A. **119**:474-477 (June 6) 1942.

337. Craig, W. M.: Role of Protruded Intervertebral Disk in Production of Low Back and Sciatic Pain, Rocky Mountain M. J. **39**:98-101 (Feb.) 1942.

338. Kaplan, A.; Bender, M. D., and Sapirstein, M.: Sciatic Pain: Its Significance in the Diagnosis of Cauda Equina Tumors; Report of Four Cases, J. Bone & Joint Surg. **24**:193-199 (Jan.) 1942.

Love [339] reports an operative mortality of 0.25 per cent in 1,600 cases of injuries to the intervertebral disks sustained in military service. He suggests that paratroopers, pilots of dive bombers and tank drivers wear a snug-fitting belt as a prophylactic measure.

McKenzie and Botterell [340] present an excellent article written from the neurosurgical standpoint. The anatomy of the three parts of the intervertebral disks, the cartilage plates, the annulus fibrosus and the nucleus pulposus, is discussed. The annulus is weakest posteriorly just off center, and it is at this point that herniation almost invariably takes place. The authors do not consider trauma alone or trauma plus degeneration wholly adequate in explaining protrusion of the disk and postulate developmental weakness as well. They explain the loss of normal spacing of the intervertebral disks in tuberculosis as due not to destruction of tissue but to the fact that the disk may bulge into the adjacent vertebral body as the cartilage plate becomes eroded. The authors think that intractable brachial neuritis may often be due to spurs or to extruded calcified disks causing pressure on a nerve root and that this pressure should be looked for more frequently. The intermittency of symptoms due to protrusion of the disks is stressed.

The authors have gradually come to the conclusion that about 95 per cent of sciatica is associated with pressure on the root of the first sacral or the fifth lumbar nerve. The diagnosis has been proved in the small percentage of cases in which there was sufficient disability to justify operation and is presumed in the ones in which the patient has been cured by conservative means or has recovered spontaneously. From a review of the neurologic signs due to protruded disks in the lower portion of the spine the authors conclude that the only important syndromes are those due to lesions between the fourth and the fifth lumbar vertebra and between the fifth lumbar vertebra and the sacrum. A lesion of the fourth lumbar disk, causing pressure on the fifth lumbar root, produces numbness or paresthesia of the inner side of the foot, a normal or diminished ankle jerk and weakness of the dorsiflexor muscles. A lesion of the fifth disk affects the first sacral root and results in numbness or paresthesia of the outer side of the foot, absence of the ankle jerk and weakness of the plantar flexor muscles. A neurologic analysis of their cases showed that when the extrusion was from the fourth disk there were no reflex, sensory or motor disturbances and that when it was from the fifth disk the ankle jerk was absent. They were unable to distinguish between lesions of the fourth or the fifth disk in about 15 per cent of the cases. On the basis of their observations they suggest that exploration may be done without preliminary myelography. They favor conservative treatment first for most patients. For simple sciatica they suggest removal of the disk alone. They believe that when there is much pain in the back spinal fusion is usually advisable, particularly in younger patients.

Overton [341] presents a good summary article with many useful details and true principles concerning the diagnosis and differentiation of the various causes of pain low in the back and sciatica, but it really contributes nothing new. The local anatomy is reviewed, the causes of pain low in the back and sciatic pain are outlined, the points of a good history are set forth in detail, and a list of fourteen physical signs to look for is given. Many of the standard manipulative tests are detailed,

339. Love, J. G.: Injuries of Intervertebral Disk in Military Service, War Med. **2**:403-409 (May) 1942.

340. McKenzie, K. G., and Botterell, E. H.: Common Neurological Syndromes Produced by Pressure from Extrusion of Intervertebral Disk, Canad. M. A. J. **46**:424-435 (May) 1942.

341. Overton, L. M.: Sciatic Syndrome, Am. J. Surg. **56**:300-307 (April) 1942.

and the differential diagnosis of a number of entities, including gout and osteoporosis, is discussed briefly. Myelography with iodized poppyseed oil is favored for localization of protruded disks.

Le Cocq [342] reports a case of sciatica due to aneurysm of the sciatic artery. The patient was a man of 68 who had pulsating sciatic pain and a visible and palpable pulsation of the right buttock synchronous with the heart beat. At operation an aneurysmal sac the size of a small orange was found in the sciatic artery. It was removed with good symptomatic results. The cause of the aneurysm was considered to be an atheromatous degeneration of the arterial wall.

XIII. CONDITIONS INVOLVING THE KNEE JOINT

PREPARED BY RALPH K. GHORMLEY, M.D., ASSISTED BY H. HERMAN YOUNG, M.D., W. H. BICKEL, M.D., PAUL R. LIPSCOMB, M.D., AND JUAN RUIZ, M.D., ROCHESTER, MINN.

Efskind [343] reviews an experimental study of the anatomy and histology of the knee. Among his conclusions should be noted that normally the synovial membrane shows distinct signs of cellular degeneration and regeneration. After synovectomy the regeneration is brought about by slightly differentiated mesenchymal cells in the connective tissue membrane. The cells of the synovial membrane do not have any capacity for formation of fibroblasts or phagocytic cells. There is an abundance of phagocytic cells in the subsynovial tissue, and Efskind suggests that the joint capsule may belong to the reticuloendothelial system.

Roentgenography of the Knee.—Wiberg [344] has found that the femoropatellar joint is best projected in a roentgenogram at 40 degrees of flexion. His study led to some conclusions regarding normal patellas, luxation of the patellas, chondromalacic patellas and arthritis deformans. By means of a detailed roentgenographic study, specially prepared specimens and a necropsy series of 25 knee joints frozen in different positions of flexion, he showed that in certain positions contact between the patella and the femoral condyle takes place over a comparatively small cartilaginous surface and that such extra stress is likely to lead to chondromalacia.

Lagomarsino and dal Lago in 1941 [345] and in 1942 [346] again review the subject of pneumoroentgenography, concluding that a preoperative diagnosis of the types of internal derangement can be made.

The Patella.—Jones and Hedrick [347] summarize and classify the various patellar anomalies that are encountered and are occasionally confused with fractures. They describe six types of anomaly, the first being a conical or triangular projection at the upper and outer quadrant of the patella. The other five types represent types of bipartite patella, the first type, which is the most common one encountered,

342. LeCocq, J. F.: Sciatica from Aneurysm of Sciatic Artery, Northwest Med. **41**:121-122 (April) 1942.

343. Efskind, L.: Experimental Study of Knee Joint Capsule: Histology and Pathology of Synovial Membrane, Acta orthop. Scandinav. **12**:214-266, 1941.

344. Wiberg, G.: Roentgenographic and Anatomic Studies on Femoropatellar Joint, with Special Reference to Chondromalacia Patellae, Acta orthop. Scandinav. **12**:319-410, 1941.

345. Lagomarsino, E. H., and dal Lago, H.: Sign of Separation of Anterior Cornu of Semilunar Cartilage in Pneumoroentgenography, Rev. ortop. y traumatol. **11**:106-123 (Oct.) 1941.

346. Lagomarsino, E. H., and dal Lago, H.: Pneumoroentgenography of Knee, Rev. ortop. y traumatol. **11**:192-216 (Jan.) 1942.

347. Jones, H. C., and Hedrick, D. W.: Patellar Anomalies: Roentgenologic and Clinical Considerations, Radiology **38**:30-34 (Jan.) 1942.

being a small fragment at the upper and outer quadrant. The second type is characterized by a vertical fissure usually observed in the lateral quadrant of the patella. There are also the rarer varieties of U-shaped patellas with a small fragment between the two arms of the U. Another type shows a transverse fissure at the lower pole, and the last type is characterized by a linear fracture at the lower pole which appears to be almost in contact with the lower margin of the patella.

Whether the multipartite patella is the result of failure of union of separate ossification centers or the result of localized osteochondritis is still a question. Jones and Hedrick believe that if it is due to osteochondritis the patella should show some evidence of end results similar to those observed in osteochondritis, namely, ultimate healing and union with the main fragment. These are not observed, and therefore, in their opinion, osteochondritis is not the cause. The other hypothesis of origin of multipartite patella is that there is a failure of union of separate ossification centers. In the differential diagnosis of patellar anomaly and fracture the history is all-important. When a fracture is present, the fracture line is usually roughened, whereas with the anomaly the line is smooth. In the anomalous patellas the adjacent surfaces of the fragments are separated fairly uniformly throughout their entire length, while after fractures the space intervening between the fragments is of varying width.

Girardi [348] studied the patellas of dogs and found that after excision in these animals there were diminished active movement in the knee, changes in the cartilaginous surfaces and atrophy of the extensor muscles. He agrees with De Vriese that the patella represents the proximal portion of an osseous element intermediate between the tibia and the fibula.

Houkom [349] reviews the results of surgical treatment of 27 dislocating patellas from the New York Orthopaedic Dispensary and Hospital. He did not find any definite causative factor. All his patients were female. In 20 cases he classified the deformity as adolescent, in 4 as congenital, in 2 as due to knock knee caused by a fracture in infancy and chondrodysplasia and in 1 as due to residual poliomyelitis. There were no cases of traumatic dislocation. Twenty-two transplants of the tibial tubercle were done, with the following results: 50 per cent excellent, 40 per cent good and 10 per cent poor. In 12 cases fascial structures were cut at the same time as the transplantation was done, with the same percentage of excellent, good and poor results. The medial capsule was plicated in 8 cases, and in 9 supracondylar osteotomy was performed, with 2 excellent, 5 good and 2 poor results.

Pellegrini-Stieda Disease.—Two papers (Hamsa [350]; Kulowski [351]) are devoted to Pellegrini-Stieda disease. [ED. NOTE.—Kulowski's paper is a carefully prepared review of the subject and should be read by any one interested.]

Wounds and Injuries of the Knee.—Mauck [352] studied 587 cases of severe acute injuries to the knee, chiefly among athletes and industrial workers. The conclusions drawn are that the primary damage is usually to the ligamentous structures

348. Girardi, V. C.: Experimental Patellectomy in Dogs, Rev. ortop. y traumatol. **11**:257-274 (April) 1942.

349. Houkom, S. S.: Recurrent Dislocation of the Patella: Study of End Results in Twenty-Seven Cases, Arch. Surg. **44**:1026-1037 (June) 1942.

350. Hamsa, W. R.: Sequel of Knee Ligament Strain: Pellegrini-Stieda's Disease (Metacondylar Traumatic Osteoma), Nebraska M. J. **27**:62-64 (Feb.) 1942.

351. Kulowski, J.: Post-Traumatic Para-Articular Ossification of Knee Joint (Pellegrini-Stieda's Disease), Am. J. Roentgenol. **47**:392-404 (March) 1942.

352. Mauck, H. P.: Severe Acute Injuries of the Knee, Am. J. Surg. **56**:54-63 (April) 1942.

and that the medial, collateral and crucial ligaments are the structures most frequently damaged. He believes that damage to the semilunar cartilages is secondary. In his opinion effusion into a traumatized knee is practically always due to hemorrhage if swelling takes place immediately, and this hemorrhage into the joint is one of the greatest factors in producing an unstable joint as well as hypermotile cartilages with subsequent locking and damage to the semilunar cartilages. He concludes that the treatment indicated is, first, the prevention of prolonged distention of the capsule; second, protection of the injured ligaments, and, third, avoidance of atrophy of disuse and maintenance of the tone of the supporting muscles, especially the quadriceps and vastus muscles.

In Mauck's series there were 416 cases of tear of the internal lateral ligament; these comprised 71 per cent of the total. This ligament is important in maintaining stability of the joint. Because of the anatomic arrangement of this ligament it is taut when the knee is in extension and relaxed in its posterior portion when the knee is in flexion. When sufficient force is exerted on this ligament with the leg in abduction or externally rotated, the anterior fibers of the lateral ligament are first to give way. The tear is usually from the tibial head and rarely from the femoral condyle. Hemorrhage into the joint keeps the tear open, eventually producing healing with a relaxed ligament. According to Mauck the early removal of the hemorrhage is one of the most important features in securing a stable knee after such an injury. An experimental procedure carried out on a fresh cadaver demonstrated that pressure within a joint kept the torn edges of the ligament separated and thus would prevent normal healing. The second most important feature in the treatment is the application of a cast hinged at the knee to allow movement while still protecting the injured ligaments. The patient is allowed to walk fairly early with this cast on, to prevent atrophy of the quadriceps and vastus muscles. The cast is worn for six weeks, and muscle exercises are carried out with the patient in the cast and for several months after its removal.

Injury to the external lateral ligament is comparatively rare. The symptoms are much the same as those of injury to the internal lateral ligament, and the treatment suggested for tear of the internal lateral ligament is recommended for tear of the external lateral ligament as well as for tears of the crucial ligament. Mauck recommends conservative treatment for acute injuries to the semilunar cartilages unless it is impossible to unlock the joint. Fractures of the tibial spine were usually treated by aspiration and fixation in a straight cast for six to eight weeks, but in about a third of the cases a hinged cast was used. Mauck believes that in the latter a better result was obtained with less atrophy and less relaxation of the joint. Simple traumatic synovitis was a rare injury in his series, produced only by a direct blow or contusion. In cases of mild traumatic synovitis a compression bandage and restricted activities were all that were necessary. In many cases what is thought to be traumatic synovitis is due to injury to the other structures.

[ED. NOTE.—Mauck's wide experience with this type of case makes this review an important contribution.]

Von Rosen [353] believes that a solitary injury to the ligaments of the knee is not encountered and that a combination of lesions, such as injuries to the anterior crucial and the medial collateral ligament and the medial meniscus, is to be expected. In cases of complete rupture of the posterior crucial ligament early suturing is recommended, because such an injury predisposes to arthritis deformans and the prognosis is more unfavorable than that of tears of the anterior crucial ligament.

353. von Rosen, S.: Diagnosis and Therapy of Injuries to the Ligaments of the Knee, Acta orthop. Scandinav. **12**:117-159, 1941.

In cases of acute injury, immobilization in a cast for as long as three months is indicated. Von Rosen thinks that in cases of long-standing injury the main disability is due to tears of the medial collateral ligament and an accompanying rupture of the anterior crucial ligament is of minor importance.

Bernstein [354] reports 5 cases of an injury to the knee joint which he says has not been reported previously in the literature. This was an elevation or stripping of the articular capsule which fits over the cartilage-coated ends of the femoral condyles. The diagnosis is made from lateral roentgenograms, which show a white line at the anterior margins of the condyles. The mechanism, according to Bernstein, is trauma to the knee causing the patella to traumatize the cartilage and the synovial reflection of the capsule. The treatment is rest and avoidance of weight bearing enforced by cast or caliper splint for six to eight weeks.

Hart [355] advocates the use of hot packs in post-traumatic treatment of joints, citing this method as the use of the "Kenny principles" in the treatment of protective spasm about a traumatized joint. [ED. NOTE.—The treatment has been used by many for a long time, certainly long before it was publicized by Sister Kenny.]

Semilunar Cartilage.—Murray [356] reviews the several features in the treatment of torn semilunar cartilages which in his opinion influence the success of surgical treatment. In 315 of 461 knee joints that had been operated on, the meniscus had been injured. Murray believes that the rapid and profound hypotonia and atrophy of the rectus and vastus muscles which follow intra-articular damage to the knee joint are not an atrophy of disuse. The nature of this phenomenon has never been determined accurately. Experimentally, it has been shown that an identical phenomenon can be produced in the extensors of the thigh of the dog by removing a meniscus from the knee joint and that its occurrence can be prevented if the knee joint is denervated before operation is done. In Murray's opinion, next to the elimination of the pathologic condition of the knee joint, the most important factor in satisfactory results with injuries of the meniscus, in regard both to the ultimate outcome and to the rapidity with which full and unlimited function can be secured, is restoration of the lost muscular tone in the extensor apparatus of the knee and elimination of the atrophy which affects the extensor muscles. It is not believed that repeated attempts should be made at conservative treatment for recurrent lesions of the meniscus.

A certain percentage of primary lesions of the meniscus undoubtedly entail tearing of the attachment of the meniscus to the lateral ligament and the adjacent capsule. The rest are tears through the meniscus itself. There are no ways of determining these two types clinically. The ligamentous tears will heal if the meniscus can be held in relation to its normal contacts by extension of the knee. Tears through the meniscus itself will not heal.

All lesions of the meniscus are treated conservatively, if possible. Only in those cases in which there is locking of the joint and in which the locking cannot be reduced while the patient is under anesthesia is primary operation urged. In cases in which locking has not occurred or in which reduction of the locking is possible, aspiration is performed if the hemarthrosis is large, and the extremity is

354. Bernstein, M. A.: Perichondral Arthropathy of Knee Joint, Am. J. Surg. **58**:279-284 (Nov.) 1942.

355. Hart, V. L.: Kenny Principles and Injuries of Knee Joint, J. A. M. A. **120**:900-902 (Nov. 21) 1942.

356. Murray, C. R.: Complicating Factors in Treatment of Injuries to Menisci of Knee Joint, Am. J. Surg. **55**:262-273 (Feb.) 1942.

then placed in extension in a circular plaster cast. Plaster is applied over stockinet only, with thin felt strip padding about essential bony points. The patient then is urged to walk as much as possible and practice quadriceps exercises at as nearly hourly intervals as possible for four weeks. The cast then is removed and the natural exercise of the extremity encouraged. Murray prefers not to use any physical therapy but depends on active motion of the joint by the patient. Three hundred and sixteen clinically certain injuries of the meniscus so treated healed completely without operation and without recurrence. He felt that had immobilization been practiced in these cases without the emphasis on use and exercise as the essential feature of the treatment, there would have been a relative instability of the knee with secondary lesions of the joint leading to prolonged disability.

When operation must be performed, the patient is instructed in quadriceps muscle exercises, which he carries out for two days prior to operation. After operation a moderately firm pressure dressing is applied for twenty-four to forty-eight hours, but patients start quadriceps muscle exercises at the end of twenty-four hours. When postoperative contraction of the quadriceps muscle is difficult to initiate, it is aided by a Smart coil to give rhythmic contraction. Voluntary bending of the knee is started when the pressure bandage is removed. The patient is up in a chair on the fourth day, is walking with crutches on the fifth or sixth day and usually leaves the hospital about the ninth day. Quadriceps muscle exercises are continued during the entire convalescence. In Murray's opinion, keeping a patient on crutches, deluging him with physical therapy and requiring postoperative immobilization of the knee joint are all conducive to delay of functional and economic rehabilitation.

The second complicating factor entering the discussion was the question of incision used. Murray has come to the conclusion that a small parapatellar incision is unwise because of the proved inability to make the diagnosis of a lesion of the meniscus as the sole pathologic condition present. In 70 per cent of the cases there have been at least two lesions, and in more than half of this 70 per cent there have been anywhere from three to eleven lesions in the joint. Murray now uses a long internal or external parapatellar incision running from the top of the quadriceps pouch to below the tibial margin. The patella then is retracted, and when the joint is flexed the entire joint is exposed. In Murray's opinion, it is only by this method that the joint can be examined completely enough to ascertain what condition is present. He has not found it necessary to repair the anterior crucial ligament in order to restore stability to a knee joint, although in 8 per cent of the cases the anterior crucial ligament was found completely torn and in 6 per cent partially torn. In general, Murray believes that injuries of the crucial ligament are handled best by intensively striving to restore muscular tone and volume and that operative repair should be reserved for those cases in which this is impossible.

The third factor in the discussion was the use of a tourniquet. Murray believes that the use of a tourniquet enforces anoxemia of the extremity below it and that in an extremity already compromised by loss of muscle tone this anoxemia is damaging. In order to alleviate bleeding as much as possible at the time the operation is performed, the patient is placed in the high Trendelenburg position with the knee joint just distal to the foot piece in the table. This effectually drains the venous circulation. When the incision in the skin is made, the bleeding points are surprisingly few in comparison with those encountered when the patient is in the flat position. They are dealt with by clamp and cautery. Towels then are clipped to the wound, incision through the capsule is made and the bleeding points are treated similarly. The synovial membrane is then opened, the patella retracted

and the foot piece of the table dropped, the thigh being left in the Trendelenburg position with the knee flexed at right angles. After operation on the interior of the joint, the knee is again extended, the patient is lowered from the Trendelenburg position to the flat position and any additional bleeding points are dealt with. In closure of the wound, the synovial membrane is left unsutured so that if any oozing occurs the fluid may escape from the joint into the surrounding tissue. A moderately firm cotton pressure bandage or Ace bandage is applied over the dressings.

Murray states that since such a procedure was adopted he has had fewer postoperative collections of fluid in a joint and less difficulty in initiating rehabilitation of the muscles. In his series of 315 cases there were but 3 postoperative infections. Two of these were in knee joints subjected to diagnostic injection of air preceding operation and occurred seven or eight years before the report. In the third case a streptococcic infection occurred during an epidemic of 5 infections of clean wounds in the service. All 3 patients recovered but with marked limitation of function.

Henderson, in the discussion, says that some of the points mentioned by Murray are controversial, such as the use of the tourniquet and the length of time required for the operation. Henderson, in reporting 343 operations performed up to 1934, with the addition of 173 cases since that time, states that in the 1934 group there was complete relief in 77 per cent, improvement in 14.4 per cent and no relief in the rest. He believes, unlike Murray, that many unsatisfactory results following removal of the meniscus are due to the fact that the anterior crucial ligament was torn or stretched at the time of the injury and that the symptoms which persisted were due to lesions of that ligament.

Graham [357] reviews 128 cases in which arthrotomy was performed for internal derangement of the knee. The operations were done on soldiers in an Australian general hospital. Because of the dust and heat, encircling bandages and pads were omitted and a light acriflavine gauze dressing was sutured over the wound. More effusion and hemarthrosis than without encircling bandages were noted, but in only 2 cases was aspiration performed. Quadriceps muscle exercises were started in twenty-four hours. The average time from operation to return to light duty was forty-two and a half days. Persistent effusion was an indication for, not a contraindication to, active function of the quadriceps muscle. Stout [358] reviews the results of operations on the knee joint in a hospital for members of the New Zealand expeditionary force. Of the patients whose cartilages had been injured, 69.7 per cent returned to full duty and 16.3 per cent to base duty and 14 per cent were sent back to New Zealand.

Mandl [359] reports on a group of 840 cases of lesions of the semilunar cartilage. Thirty per cent of the series lacked the history of severe trauma, and Mandl believes that most tears of the semilunar cartilage are pathologic fractures. Rupture of the medial meniscus was eight times more frequent than that of the lateral meniscus, but cysts were more common in the lateral cartilage. Mandl recommends surgical removal in all cases of torn semilunar cartilage. He recommends a short longitudinal incision and local anesthesia and never uses a tourniquet.

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357. Graham, R. V.: Preliminary Report on Internal Derangements of the Knee Joint Treated at an Australian General Hospital, Australian Imperial Force Abroad, to May 31, 1941, Australian & New Zealand J. Surg. **11**:185-196 (Jan.) 1942.

358. Stout, T. D. M.: Rupture of Semilunar Cartilages of Knee Joint, Osteochondritis Dissecans and Hallux Valgus and Rigidus: Results of Operative Treatment and Significance of These Disabilities in Second N. Z. E. F., New Zealand M. J. **41**:130-133 (June) 1942.

359. Mandl, F.: Observations and Problems on Operation for Lesions of Semilunar Cartilage, J. Internat. Coll. Surgeons **5**:63-68 (Jan.-Feb.) 1942.

Dunlap [360] has modified the Lowe-Breck knife for removing semilunar cartilages, making it more curved and making the cutting edge V shaped instead of U shaped.

Hauser [361] reports an average of 80 to 90 per cent cure after operation for tear of the semilunar cartilages. He reports 4 cases illustrating the fact that loose bodies derived from the semilunar cartilages may be present in the joint. These loose bodies are pieces of cartilage that are lying free within the joint and may occur at the time of initial injury or may occur at a later date with repeated trauma to the cartilage. Unless the joint is examined thoroughly, some of these "joint mice" may be missed and produce an unsuccessful end result. Hauser believes that removal of the entire meniscus is indicated in all cases of fractured semilunar cartilage in order to make sure that all of the cartilaginous tissue has been accounted for and that some does not remain in the joint.

Deformities of the Knee.—Abbott and Gill [362] review the cause and treatment of valgus deformities of the knee occurring as a result of injury of the lower femoral epiphysis in childhood. The epiphysis fuses in its lateral position but continues to grow on the medial side and thus causes the valgus deformity of the knee. The degree of valgus depends on the exact location of the injury; the more lateral the injury, the greater the deformity because of the greater pivoting action. Likewise the younger the child at the time of injury, the greater the deformity. The longitudinal downgrowth of the medial condyle never equals that on the normal side, and actual shortening occurs. When the medial side of the cartilage fuses, the deformity is fixed. In addition to actual loss of length there is decreased functional length because of the valgus of the knee. There may also develop a secondary varus deformity of the upper end of the tibia, which is compensatory. The development of the femoral articular surfaces is undisturbed, but the plane of motion in relation to the shaft of the femur is altered; thus motion of the knee may be entirely normal. The soft structures on the lateral side of the thighs, including the peroneal nerve, become relatively short, and may constitute an obstacle to the correction of the deformity.

The problem of suggested treatment for far advanced deformity is to secure complete correction with as much increase of the length of the leg as possible. Normal function of the knee should be maintained, and any residual inequality of the length of the legs may be eliminated by leg lengthening or shortening operations. The procedure may be varied in two ways: 1. A triangular section of bone with its base facing inward may be removed from the medial side of the femur. This constitutes cuneiform osteotomy. 2. Osteotomy may be performed at the same level but wedged and held open on the lateral side with a bone graft from the ilium. The latter type of osteotomy gains more length than cuneiform osteotomy. Abbott and Gill stress the importance of roentgenograms of both legs and of making a plan ahead of time as to the angle of the osteotomy and how much correction is to be done. A similar osteotomy may be necessary to correct the virus deformity of the upper end of the tibia.

The greatest obstacle to full correction is the shortness of the peroneal nerve. Abbott and Gill use pin fixation in doing osteotomy. One pin holds the iliac graft

360. Dunlap, K.: Method for Complete Removal of Semilunar Cartilage, J. Bone & Joint Surg. **24**:929-931 (Oct.) 1942.

361. Hauser, E. D. W.: Loose Body of Knee Derived from Meniscus, J. Bone & Joint Surg. **24**:307-310 (April) 1942.

362. Abbott, L. C., and Gill, G. G.: Valgus Deformity of Knee Resulting from Injury to Lower Femoral Epiphysis, J. Bone & Joint Surg. **24**:97-113 (Jan.) 1942.

in place, and the other two pins hold the knee in the corrected position. If full correction is not possible at the time of the operation owing to tightness of the peroneal nerve, the deformity is corrected as much as possible, the graft held in place with pins and a spica cast applied. Three weeks later the pin holding the graft is withdrawn and the cast wedged to correct the deformity further. It is possible to gain about 2 inches (5 cm.) in some cases by double osteotomy. For growing children the authors advocate repeated osteotomy if necessary, to prevent the development of severe deformity, the final correction being done at the time of the closure of the epiphysis. For the growing child osteotomy should be performed before the medial condyle has overgrown the lateral condyle by more than ¾ inch (2 cm.). Repeated osteotomy in childhood gives added length with each operation. The deformity is never allowed to become severe, and correction is thus obtained more easily. Abbott and Gill advocate arrest of growth of the corresponding epiphysis of the normal leg before the normal femur has overgrown the involved femur by 2 inches (5 cm.), provided the final height is satisfactory with this loss of growth.

Irwin [363] reviews the deformity of genu recurvatum which sometimes follows poliomyelitis. He has found two types. The first is caused by loss of power of the quadriceps muscle and inability to lock the knee in extension. Structural changes of the bone obeying Wolff's law develop. The condyles of the femur become elongated and the angle of the tibial plateau becomes more acute than normal. The second type is caused by weakness of the calf and hamstring muscles, and the soft tissue becomes stretched. Operative treatment is successful only for the first type. Irwin corrects the deformity of the bone by wedge osteotomy of the tibia and fibula just below the epiphysial line. The proximal tibial fragment is controlled by a Kirschner wire incorporated into the spica cast. The second operation attacks the cause of the deformity by transplantation of the hamstrings into the patella.

Fitzgerald [364] describes a method of overcoming flexion deformities of the knee by applying modified Russell traction. The leg is placed on an adjustable Braun splint with a pin through the os calcis and a sling just below the knee. Russell's traction is applied with a 7 pound (3.2 Kg.) weight. The foot of the bed is elevated. As the flexion deformity is overcome, the Braun splint is lowered so that the component forces applied to the leg pull in its long axis.

Young [365] states that the problem of the fractured femur is the problem of the stiff knee. The stiffness may be due to disuse, immobilization or sepsis or to a combination of these three. Disuse is the most common and important cause and most easily prevented. Young advocates motion within the first six weeks after operation, if possible. He describes a simple mechanical apparatus whereby the patient actively sends the knee against the resistance of a counterpoising weight. In 34 cases of fracture of the femur, 18 patients were treated with early movement of the knee and 16 without early movement of the knee. In the former group there was an average of 115 degrees of flexion at six months, but in the latter there was only 35 degrees of flexion.

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363. Irwin, C. E.: Genu Recurvatum Following Poliomyelitis: Controlled Method of Operative Correction, J. A. M. A. **120**:277-280 (Sept. 26) 1942.

364. Fitzgerald, F. P.: Reduction of Old-Standing Dislocation of Knee Joint, Brit. M. J. **2**:542 (Nov. 7) 1942.

365. Young, R. H.: Prophylaxis and Treatment of Stiff Knee Following Fracture of Femur, Proc. Roy. Soc. Med. **35**:716 (Sept.) 1942.

Blair [366] describes an operation for stabilizing knees having torn crucial and collateral ligaments with four strips of fascia 12 inches by 1 inch (30 cm. by 2.5 cm.), fixed from the tibia and the fibula to the muscles and fascia of the thigh so that two cross at the fixed point of the femoral condyle. Six cases are reported, with 5 good results.

Unusual Lesion of the Knee.—Key and Large [367] report a case of histoplasmosis or reticuloendothelial cytomycosis, a condition caused by Histoplasma capsulatum of Darling. Darling discovered the organism in 1906 and pointed out its similarity to the Leishman-Donovan body of kala-azar. This case is the only one in which a joint has been found involved. The clinical diagnosis was a low grade pyogenic or a fulminating tuberculous infection. Amputation was done, but the patient died of pneumonia.

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366. Blair, H. C.: Simple Operation for Stabilization of Knee Joint, Surg., Gynec. & Obst. **74**:855-859 (April) 1942.

367. Key, J. A., and Large, A. M.: Histoplasmosis of Knee, J. Bone & Joint Surg. **24**:281-290 (April) 1942.

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